

MEETING
STATE OF CALIFORNIA
AIR RESOURCES BOARD
SCIENTIFIC REVIEW PANEL

JOE SERNA, JR., CAL/EPA HEADQUARTERS BUILDING
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SIERRA HEARING ROOM
SACRAMENTO, CALIFORNIA

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9:34 A.M.

JAMES F. PETERS, CSR, RPR
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APPEARANCES

PANEL MEMBERS

Dr. John Froines, Chairperson

Dr. Paul Blanc

Dr. Craig Byus

Dr. Gary Friedman

Dr. Katharine Hammond

Dr. Joseph Landolph

Dr. Charles Plopper

REPRESENTING THE AIR RESOURCES BOARD:

Mr. Jim Behrmann, Liaison, SRP

Mr. Peter Mathews

REPRESENTING THE DEPARTMENT OF PESTICIDE REGULATION:

Dr. Tobi L. Jones, Assistant Director

REPRESENTING THE OFFICE OF ENVIRONMENTAL HEALTH HAZARD
ASSESSMENT

Dr. George Alexeeff, Deputy Director

Dr. Melanie Marty, Chief, Air Toxicology and Epidemiology
Section

Dr. Andrew Salmon, Chief, Air Toxicology and Risk
Assessment Section

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1 PROCEEDINGS

2 CHAIRPERSON FROINES: This officially opens the
3 meeting of February 28th, 2008. And we're going to have a
4 slight change in the process.

5 The third item on the agenda that deals with
6 priority setting, we're not going to hold that today.
7 Roger Atkinson, who was going to be one of the speakers,
8 has resigned from the Panel. And we will hold that at the
9 next -- we will hold the priority-setting workshop at the
10 next meeting and finish it off. But we need to obviously
11 replace Roger in some capacity. So the third item on the
12 agenda won't occur today.

13 And so we're going to start with Endosulfan. And
14 I just wanted to -- I feel that the Endosulfan issue is --
15 it's like living again in 1962 with Rachel Carson. And I
16 just wanted to read something from ATSDR, which says,
17 "Currently the GABA antagonism mechanism of toxicity is
18 the most widely accepted hypothesis." This is the same
19 mode of action that ATSDR has identified for lindane,
20 aldrin, dieldrin, and chlordane. These pesticides are no
21 longer used for agriculture in the United States.

22 So Endosulfan is a compound which in a sense is
23 at the bottom end of a series of compounds which have been
24 eliminated. And so hopefully over time this compound will
25 become even less used. So I wanted to just say that at

1 the outset to put it in context.

2 What I'd like to do then is to invite Tobi Jones
3 from DPR to make a short presentation. And then I'd like
4 to have a discussion among the Panel about voting on the
5 document in terms of its being a toxic air contaminant and
6 then to get on with the findings.

7 So, Tobi, please.

8 DPR ASSISTANT DIRECTOR JONES: This is Tobi
9 Jones, DPR. I want to make a few introductory comments to
10 review where we are on the Endosulfan risk assessment.

11 The Panel discussed earlier drafts of the
12 Endosulfan report at its meetings in September and
13 December. And the draft before you today incorporates
14 changes suggested in those meetings.

15 We've provided you with a revised document -- and
16 I hope that our annotations are clear in this copy that we
17 provided you -- that address the areas discussed.

18 The current version includes: 1) Changes in the
19 exposure estimates for bystanders; 2) more detail on the
20 reported illnesses; and 3) certain changes in the
21 occupational scenarios.

22 The fourth area is an expanded discussion of
23 studies on genotoxicity and oncogenicity and includes an
24 additional NTP, a mouse study. In this area we have
25 attempted to maintain consistency with OEHHA's findings.

1 We are making some minor refinements in the executive
2 summary and the risk assessment text beyond what you all
3 have received regarding genotoxicity and tumor promotion
4 based on some very recent discussions with Dr. Landolph.
5 It would be acceptable to DPR if the Panel identifies
6 further research needed in its findings.

7 The fifth area is an expanded discussion of
8 studies that pertain to an additional uncertainty factor
9 for age-related effects. We have not reached agreement
10 with OEHHA on the rationale for this additional
11 uncertainty factor. But we'll continue to discussion with
12 them the approach that they've taken.

13 Should the Panel determine that it recommends the
14 use of an additional uncertainty factor, DPR would welcome
15 the Panel's guidance.

16 In conclusion, we believe we have presented a
17 defensible case that Endosulfan should be listed as a
18 toxic air contaminant. DPR and OEHHA are in agreement
19 with the endpoints that form the basis of our proposal.
20 We hope that the Panel agrees with our proposal and we
21 look forward to receiving your findings.

22 Let me conclude by also expressing our
23 appreciation for the Panel's review of the document and
24 especially the helpful comments of Drs. Landolph, Hammond,
25 and Atkinson in refining the risk assessment.

1 CHAIRPERSON FROINES: Thank you very much.

2 My own point of view is I think there's very
3 ample evidence of Endosulfan being a toxic air
4 contaminant. But let me turn it to Joe and Kathy, who
5 were the leads on the compound, and get their perspective
6 for the rest of us.

7 PANEL MEMBER HAMMOND: Thank you.

8 I would like to thank you, Tobi, and your staff
9 for the work you've done, and OEHHA for the work that they
10 have done. I think there's been a lot of work that's been
11 done on this compound, and I think the staffs have been
12 responsive to the comments from the Science Review Panel.
13 And Joe and I have been working on some of the findings
14 for that.

15 And do we want to go directly to the findings
16 then at this point?

17 CHAIRPERSON FROINES: We're still at whether it's
18 a TAC stage.

19 Paul last night asked me, "Don't we do TAC and
20 findings at the same time?" But the answer is we
21 generally vote on the document as a TAC and then go to the
22 findings.

23 And I had one question for the two of you. Joe
24 and Kathy, has everybody on the Panel seen the findings?

25 Oh, that's a serious problem.

1 PANEL MEMBER HAMMOND: Yeah, right.

2 CHAIRPERSON FROINES: Peter, do you have the
3 findings.

4 PANEL MEMBER HAMMOND: So in terms of the toxic
5 air contaminant, I think that it's our feeling, and I
6 think I would like to move on behalf of the Science Review
7 Panel, that there is ample evidence that Endosulfan is a
8 toxic air contaminant.

9 Do I make that as a motion? Is that the
10 procedure?

11 CHAIRPERSON FROINES: You can. But --

12 PANEL MEMBER HAMMOND: But that's the
13 procedure --

14 CHAIRPERSON FROINES: No, but you -- I mean we
15 want to hear what you think, and then you can make a
16 motion as a result of that. I would make the motion after
17 we've gone around the room --

18 PANEL MEMBER HAMMOND: Oh, okay.

19 CHAIRPERSON FROINES: -- so that everybody has a
20 chance to talk.

21 PANEL MEMBER HAMMOND: All right. So there are
22 several different endpoints where Endosulfan has been
23 shown -- demonstrated to be a toxic air contaminant. And
24 there have been some measurements in the air that indicate
25 that the levels to which people can be exposed fulfill the

1 requirements of something being a toxic air contaminant.
2 So there's both toxicity and exposure data that support
3 that.

4 So I personally find the evidence compelling that
5 Endosulfan's a toxic air contaminant.

6 CHAIRPERSON FROINES: Joe.

7 PANEL MEMBER LANDOLPH: Yes, I pretty much concur
8 with Dr. Hammond's discussion. It's a neurotoxicant.
9 It's a genotoxicant. There's some suggestion that it does
10 things in vitro which might lead it to be a tumor
11 promoter. More work needs be done on carcinogenicity.

12 But I was particularly impressed that some of the
13 applicators were occasionally getting neurotoxicological
14 symptoms. And that worried me from the beginning.

15 So adding all these things together -- it also
16 seems to be endocrine disrupter, it causes problems in
17 development. So for all these reasons, I would second Dr.
18 Hammond's opinion. My opinion is the same and I'm
19 confident that, in an assessment from me, that it is a
20 toxic air contaminant, yes.

21 CHAIRPERSON FROINES: So, Charles.

22 PANEL MEMBER PLOPPER: I don't have anything to
23 add. I'd concur with that. I think there's pretty good
24 strong evidence that it is.

25 CHAIRPERSON FROINES: Gary.

1 PANEL MEMBER FRIEDMAN: I agree with Charles. I
2 have nothing to add. And I think their conclusions are
3 very reasonable.

4 CHAIRPERSON FROINES: Craig.

5 PANEL MEMBER BYUS: Yeah, I agree. I think the
6 leads have done a fine job on this with DPR and as well as
7 OEHHA's input. And I also agree.

8 CHAIRPERSON FROINES: Paul.

9 PANEL MEMBER BLANC: I think there are two parts
10 to the formulation here. And I want to make sure that the
11 record also indicates that not only is the chemical under
12 discussion inherently toxic, but also that there is
13 convincing evidence of airborne exposure to the toxin at
14 levels which would pose a potential health risk even
15 within the somewhat more restrictive guidelines of the DPR
16 calculation approach. So that it's a two-pronged issue.

17 CHAIRPERSON FROINES: And the second prong is?

18 PANEL MEMBER BLANC: Well, the first prong,
19 everyone said it's clearly a toxic material. The second
20 prong is not only is it a toxic material, but there's
21 airborne exposure at levels which make it a toxic air
22 contaminant. After all, it wouldn't be a toxic air
23 contaminant if it wasn't in the air.

24 CHAIRPERSON FROINES: There's actually some new
25 data emerging on that issue. But it's not in the record

1 so I won't bring it up. But the point is actually getting
2 stronger rather than weaker.

3 We went around the room so fast. I don't want
4 to -- Melanie, are you comfortable with the conclusions
5 the Panel has made as the OEHHA person?

6 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF
7 MARTY: Sure.

8 CHAIRPERSON FROINES: I don't know if we've ever
9 had something quite so --

10 PANEL MEMBER BLANC: Well, again, I think that
11 it's partly because some of the issues that -- some of the
12 nuance that may come up in the wording of what the content
13 of the findings -- our findings and interpretation
14 themselves are probably still worthy of discussion. And
15 I'd have to go back and look at the record. I'm actually
16 not sure that we -- you know, that we typically have very
17 much difficulty with the phase of the dichotomous yes/no.
18 Some of the more protracted discussions occur related to
19 content of the -- more emphasize in the findings
20 statement.

21 So I certainly would be comfortable moving that
22 the Scientific Review Panel concurs that the scientific
23 evidence presented supports designating this compound as a
24 toxic air contaminant.

25 CHAIRPERSON FROINES: Is there a second?

1 PANEL MEMBER HAMMOND: I second that.

2 CHAIRPERSON FROINES: Is there a discussion?

3 PANEL MEMBER BYUS: John, don't we -- at some
4 point I mean I agree. But don't we also have to say
5 whether the document is seriously deficient or not? Or is
6 that part of the findings? Where is that?

7 CHAIRPERSON FROINES: We absolutely have to make
8 that determination. And that will -- that is a
9 requirement of our findings.

10 PANEL MEMBER BYUS: Okay.

11 PANEL MEMBER BLANC: And actually that's why I
12 worded my motion the way I did, which is that whatever the
13 deficiencies may be, I believe that the science is
14 acceptable to the standard of the dichotomous designation
15 of yea or nay to it being a toxic air contaminant.

16 CHAIRPERSON FROINES: Paul was actually making --
17 you see, we don't determine -- we may recommend that it be
18 a TAC, but we absolutely have to determine the adequacy.
19 And so that's what I heard him doing. And so if everybody
20 understands that, then we can --

21 PANEL MEMBER BLANC: Could you read back the
22 wording is that possible.

23 (Thereupon the record was read as requested.)

24 PANEL LIAISON BEHRMANN: Dr. Froines?

25 CHAIRPERSON FROINES: Yes.

1 PANEL LIAISON BEHRMANN: If I could just add very
2 briefly -- I'm Jim Behrmann, Staff Liaison for the Panel.

3 The Panel most often meets in northern and
4 southern California. And I want to thank the Panel for
5 meeting here in Sacramento today. And for the benefit of
6 the people that are here today that are not normally at a
7 panel meeting, I wanted to just add -- and I'm sure you
8 may even have alluded to it in your earlier remarks -- but
9 lest anyone here in the audience think that the staff has
10 not had to present much in the way of evidence or that the
11 Panel hasn't really discussed this. This report has
12 actually been the subject of two previous meetings, at
13 which -- during which time there were hours of discussion
14 by the Panel members, both in September and in December.

15 So I wanted to make sure that the people
16 attending today that do not normally have the benefit of
17 seeing this Panel, that they get the correct impression
18 that this isn't an easy task to come before you.

19 Thank you.

20 CHAIRPERSON FROINES: What he's really saying is
21 that "too bad, folks, but you've missed all the fun."

22 (Laughter.)

23 CHAIRPERSON FROINES: So all in favor?

24 (Ayes.)

25 CHAIRPERSON FROINES: Opposed?

1 It's unanimous.

2 So thank you, Tobi. You're done. We're in
3 business.

4 Now the question comes, do we want to take a
5 10-minute break, 15-minute break and give people a chance
6 to read the findings as they're currently written?

7 PANEL MEMBER FRIEDMAN: You know, I don't -- I'm
8 sorry that I keep harping on this. But my experience in
9 the past is the findings are not -- I just opened a page
10 at random that says, "Since this was an older study a
11 number of developmental markers were not as assayed
12 including sperm counts, crown rump links, skeletal stains,
13 vaginal opening, and preputial separation." That should
14 not be part of our findings, I don't -- I think we should
15 have a brief, maybe two-page document. And that was my
16 experience in the past.

17 This is regurgitating a lot of the larger report.
18 And I'm not sure that that's what's expected from us and
19 what's helpful.

20 CHAIRPERSON FROINES: Well, my view is that we
21 have -- I think -- by the way, Kathy and Joe would agree
22 that this is too long. So that it's a friendly audience.

23 My view is that the findings should be exactly
24 that. They should be findings. In other words, they
25 should be the written justification for our decision of

1 the compound as a toxic air contaminant. In other words,
2 we don't need extraneous material that doesn't pertain to
3 the actual decision that we made. We made a decision to
4 identify this as a toxic air contaminant, and there were
5 reasons for that. And I think our findings should be
6 those reasons.

7 PANEL MEMBER FRIEDMAN: I agree. But do we need
8 all this detail?

9 CHAIRPERSON FROINES: No, no. No, we don't.

10 PANEL MEMBER FRIEDMAN: And I don't think we can
11 read this in 10 or 15 minutes, frankly.

12 CHAIRPERSON FROINES: Well, what would you
13 suggest?

14 PANEL MEMBER FRIEDMAN: Well, you know, in view
15 of saving resources, I'm not suggesting that this be
16 rewritten. But, you know, in the future I would like to
17 see us go back to what we used to do and have like a
18 two-page summary that justifies the conclusion that it's a
19 toxic air contaminant and here are the reasons why.

20 CHAIRPERSON FROINES: I'll tell you this. I saw
21 an Email from Joe in which he went through the process of
22 how this has emerged. It went to Kathy, it went to Joe,
23 it went to Kathy, it went to Joe. And so he went through
24 that process. And then at the end he said, "And finally
25 it will go to John." That's the -- "we're going to get

1 rid of it and send it off to Froines and let him deal with
2 it."

3 So I'm happy to be the person -- well, I'm not
4 happy to be the person. But I'm willing to be the person
5 who will take what they have written and write an edited
6 version, if that would be acceptable, based on what we're
7 going to talk about today. And I don't know whether you
8 want to take a break and talk about it or whether you want
9 to leave it up to me or how you would like to approach it.
10 But I'm going to -- I will do exactly what you want,
11 because I think -- I think what we want is findings that
12 give the context for the decision. And we are in complete
13 agreement I think.

14 PANEL MEMBER FRIEDMAN: Okay. Well, you know, I
15 hate to assign you work out, because I'm not in the
16 position. But I think that would be great, if you take
17 this and make it into the kind of findings we used have
18 that were about two pages and had the main points of why
19 it's a toxic air contaminant, why people are exposed to
20 it.

21 CHAIRPERSON FROINES: See, I get \$110 a meeting.

22 (Laughter.)

23 PANEL MEMBER FRIEDMAN: In that case, absolutely
24 you should do it.

25 CHAIRPERSON FROINES: Yeah. See, I get the extra

1 10.

2 That's not true, by the way.

3 PANEL MEMBER BLANC: Can I just point out one
4 nuance here to what's being discussed, which is that,
5 Gary, although I would agree with you 110 percent in terms
6 of the kinds of findings that we deal with with the
7 proposals that come from OEHHA or, you know, the work that
8 comes from them, I think that the Department of Pesticide
9 Regulation, as we have been struggling to evolve to a
10 common ground, it may be necessary for our findings to be
11 somewhat less telegraphic than they might need to be for
12 the other. So that there may be some bifurcation here.

13 Not that it has to be perhaps as elaborate as
14 this. But I think that there are certain -- there are
15 certain areas, for example, in which there was certainly
16 considerable debate and in the end no final closure
17 between OEHHA and DPR on key issues. And I think that
18 although that's not going to prevent us from finding
19 that -- it has not prevented us since we've just moved
20 that this does meet scientific muster to establish it as a
21 toxic air contaminant. In fact, it maybe quite important
22 for us as a panel not to have our lack of explicit comment
23 on certain issues be misinterpreted as leaning towards
24 some particular interpretation of the approach.

25 I mean I hope I'm not being too long winded in

1 what I'm trying to say.

2 PANEL MEMBER FRIEDMAN: Well, I have no problem
3 with that. We definitely should include our comments, but
4 not regurgitate little reviews of studies and what --

5 PANEL MEMBER BLANC: No, no, no. But I'm just
6 making the point that I think whatever this -- whatever
7 John working with Kathy and Joe comes to terms with an
8 edited-down version of this, it will still likely, I
9 anticipate, be longer than the two-page ideal findings
10 that you're referring to. Perhaps that would be
11 reasonable in terms of certain of the other items that
12 we've dealt with historically.

13 CHAIRPERSON FROINES: I should also add something
14 that Tobi alluded to in her remarks and, that is, that our
15 findings are going to have some differences between what
16 we write and what DPR has written. We're going to
17 deal -- we are going to comment on the children's safety
18 factor, for example. Tobi alluded to the genotoxicity and
19 carcinogenicity issue that Joe's raised in the past.

20 So there are going to be -- our findings are
21 going to have our stamp of approval. They're not a
22 watered-down version of DPR or OEHHA's findings; and
23 that's what I really want to avoid for ourselves. I think
24 our findings should have our stamp of approval on what we
25 think about this chemical. And so that's what it will

1 reflect. And if that -- but I do think there are
2 substantial cutting that can actually occur. And it may
3 not be two pages, according to what Paul said, but it
4 could be.

5 PANEL MEMBER FRIEDMAN: And I think -- well, I
6 totally agree with you. And I think this will be a more
7 useful document to the people -- to the Air Resources
8 Board if it is cut and it's readable and our conclusions
9 and our comments are clearly stated, rather than going
10 through all this massive regurgitating literature.

11 CHAIRPERSON FROINES: Joe.

12 PANEL MEMBER LANDOLPH: Yeah, I do have to
13 apologize a little bit. It was a little bit difficult for
14 Kathy and I and John to converge for various time
15 constraints. So it's been a work in progress. And I was
16 working on it yesterday for the second time at 11:30, and
17 I think I finally Faxed -- Emailed it to John. So we view
18 it as a work in progress shrinking it. And we just didn't
19 get enough time to shrink it down further.

20 I don't think it's going to hit two pages. I
21 agree with Paul. But it certainly can go down more from
22 the nine. Maybe four or five or something like that.
23 There's a lot of elegant details that we don't want to
24 sacrifice. Some of it backs up the conclusions of
25 neurotoxicity and genotoxicity, et cetera. But we

1 certainly can shrink it down more, no question about it.

2 CHAIRPERSON FROINES: And I actually think that
3 the developmental and reproductive and neurotoxicity are
4 the three central areas that -- in a sense the oncology
5 and the genotoxicity has gotten the bigger play. But it's
6 less -- in some level less important -- not less important
7 but just has less evidentiary basis.

8 I guess what I'm saying is that we're going to
9 take -- the three of us are going to take this document,
10 do a new version, submit -- circulate it to the Panel.
11 And when we come into the next meeting, we spend 30
12 seconds on approving it and that's it. So we basically do
13 it by communication among the Panel as we go. And
14 Gary -- so we'll have it down to a size that Gary won't
15 come in to the meeting and say, "Whoops, you guys didn't
16 listen to a word I said."

17 Is that -- so we won't try and take a 10-minute
18 break or a 15-minute break, because I think you don't get
19 good work that way. Is that reasonable?

20 PANEL MEMBER FRIEDMAN: And I'd like to add
21 that -- you know, I don't mean this at all as criticism of
22 the lead people who -- you know, you guys have done a
23 tremendous job. You've found a lot of flaws and problems
24 that have been, you know, dealt with by DPR, and I want to
25 thank you for all the good work you've done. I sort of --

1 that's what one of my pet peeves in life is brevity. And
2 I guess I'm bringing that here.

3 CHAIRPERSON FROINES: Tobi, are you okay with --
4 this isn't going to throw you off, is it?

5 DPR ASSISTANT DIRECTOR JONES: That's okay.

6 CHAIRPERSON FROINES: The good news -- the bad
7 news, it will be moved -- it won't be finished till next
8 time. But the good news is that it will be finished next
9 time. And that's what we want.

10 PANEL MEMBER BLANC: I think what would be useful
11 though since we're obviously going to be saving time here
12 not taking a break and not having a lengthy discussion of
13 this with the wording of the findings -- I think that it
14 would be useful for me, and I assume for the other Panel
15 members, to hear briefly from Melanie in a sort of
16 highlight form -- they've provided us also with their
17 findings. And I think it would be useful for me to hear
18 in five minutes what OEHHA sees as the outstanding gaps
19 between the two positions at this point, just so that I
20 can put that in context.

21 CHAIRPERSON FROINES: Melanie, can you do a
22 five-minute gap?

23 I should say, Paul, one of the things that's
24 important to note is that when Melanie's finished this,
25 George and Melanie and whoever else is going to present is

1 going to present the non-cancer risk assessment. And that
2 won't be voted on today. But it has an extensive amount
3 of discussion on the risk assessment vis-a-vis children.
4 So that OEHHA's position is actually coming in about 20
5 minutes and it's in considerable detail.

6 Melanie.

7 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

8 MARTY: Melanie Marty from OEHHA.

9 We did develop a revised findings recently to
10 reflect the changes that DPR made in their document. I
11 think it's safe to say that most of the things have been
12 resolved. The outstanding area of disagreement is whether
13 there's an additional factor is called for to protect
14 early life exposure. So that's really all that is left.

15 We felt that the data say there's a lot of arrows
16 pointing to inhalation being an important route of
17 exposure, being different pharmacokinetically than orally.
18 So that should play into your -- into how you're looking
19 at the data in terms of exposure.

20 And then also there are many arrows pointing to
21 potential developmental toxicity including potential
22 endocrine disruption and male reproductive toxicity that
23 came from a lot of different studies. And while none of
24 those studies is perfect in and of themselves, if you take
25 the 10,000-foot view and look at all the data, it really

1 is saying to us that Endosulfan causes male reproductive
2 toxicity in gestational and perinatal exposures. So
3 that's --

4 CHAIRPERSON FROINES: That's very useful, because
5 Joe and Kathy and I can focus on those bullets and it will
6 be in the transcript. So we'll have -- having bullets
7 like that are actually quite useful, because it helps
8 focus your...

9 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF
10 MARTY: And some of the other data indicates also that
11 effects were seen on a variety of parameters related to
12 testicular function at lower doses in younger animals than
13 in adult animals. So, you know -- and, again, none of the
14 data are perfect, so there's, you know, judgment that has
15 to come into play. But we would say that the younger
16 animals were more susceptible.

17 CHAIRPERSON FROINES: Would you send us some
18 references if you think that -- or point out where in the
19 document that those references are so we know -- to help
20 us know where to look.

21 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF
22 MARTY: Sure. Yeah, we can just send you the references
23 that we think point these issues out.

24 PANEL MEMBER BLANC: Do you think that an
25 important piece of that argument is the very recent

1 caballero study, or was that just sort of an aside?

2 Because clearly that was too leg breaking to be in the
3 document, but we could easily make sure that that enters
4 into our record.

5 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

6 MARTY: Yes, the caballero study, which just was published
7 I think last month --

8 CHAIRPERSON FROINES: That's not Roberts', right?

9 OEHHA DEPUTY DIRECTOR ALEXEEFF: No. That's an
10 additional study.

11 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

12 MARTY: No, it's an additional study. Which, you know,
13 obviously DPR couldn't put that in their document. It
14 wasn't published yet. But, you know, it does show
15 developmental neurotoxicity.

16 It's sort of, you know, interesting endpoints and
17 it's hard to know what it means. But it was clearly
18 there. It impacted the neurotransmitter concentrations in
19 various parts of the brain when Endosulfan was given
20 during gestation.

21 OEHHA DEPUTY DIRECTOR ALEXEEFF: Can I comment?

22 George Alexeeff with OEHHA.

23 I just wanted to say I think both OEHHA and DPR
24 staff have spent a lot of time trying to break through new
25 ground here, where in many cases factors are thrown in by

1 various organizations without a lot of justification. And
2 a lot of effort was spent by both OEHHA staff, DPR staff,
3 jointly and separately, trying to look at the data to
4 really understand everything from the overt results, the
5 results studied in guidelines studies, the results studied
6 in much smaller university-based studies, and trying to
7 put all the pieces together.

8 So I think what you see is probably both
9 excellent approaches by both staffs in trying to -- I mean
10 all the pieces are not there. So we're looking at a
11 puzzle where many pieces are there and we're trying to
12 explain the puzzle.

13 And so I think that's -- I think both staffs made
14 excellent efforts in that line. And that's all I wanted
15 to say.

16 CHAIRPERSON FROINES: That's great.

17 Thank you very much.

18 And I should say that I think Joe and Kathy
19 really worked their tails off on this. And so as much as
20 I agree with Gary about shortening it, they really read
21 everything and they really did work very hard to get the
22 findings for this meeting. And so it's no reflection on
23 them that we're going to shorten it to some extent.

24 PANEL MEMBER BLANC: Can I just follow up. And I
25 don't want to badger the issue, but I want to make sure

1 that I understand OEHHA's position in terms of this
2 recently emerged data. I mean your findings suggest that
3 were one to rely on the recent caballero study, it would
4 generate an RCD that would be .06 as opposed to the .194,
5 which is three times lower. That would seem to be a very
6 cogent argument for a threefold safety factor.

7 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF
8 MARTY: Yes.

9 PANEL MEMBER BLANC: And then you make a further
10 argument that in fact that's an oral study, adding further
11 uncertainty, which would seem to support an argument for a
12 tenfold safety factor, simply based on alternative or
13 emerging data that are there, leaving aside whether or
14 not -- and if those data were confirmed in other studies,
15 then you wouldn't need the safety factor because you'd
16 have the sensitive age establishing. You'd just used
17 that.

18 Is that -- am I understanding the thought process
19 correctly?

20 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF
21 MARTY: Yes, I think that's a good summation. You know,
22 part of the issue of the caballero study is the first
23 study that's actually done such a type of measurement. So
24 we know it's neurotoxic to us. Anything that's neurotoxic
25 raises a big red flag for developmental. I can't think of

1 any neurotoxin that's not worse during development than in
2 adults. So that raised a red flag immediately to us.

3 This new study, which looked at neurotransmitters
4 in the prefrontal cortex of the brain found a significant
5 difference in the Endosulfan-treated -- the pups of the
6 Endosulfan-treated dams relative to the controls.

7 So, you know, translating into that now what that
8 means, you know, I can't say what that actually means.
9 But, you know, neurotransmitters participate in
10 neuro-development and they're very important signaling
11 molecules. So that raises -- makes the red flag a little
12 bigger, I guess I should say.

13 So I'm not sure we -- you know, it's hard for me
14 to say we would base our number on that study.

15 PANEL MEMBER BLANC: No, I'm not saying that
16 either. I'm saying that it's -- in support of the
17 argument for the safety factor. If you were basing your
18 numbers on this, you wouldn't have a safety factor because
19 you would say this is what you've shown in the sensitive
20 age range.

21 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

22 MARTY: Right.

23 PANEL MEMBER BLANC: Isn't that correct?

24 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

25 MARTY: That's right. If we had a good strong

1 developmental database, we would use that instead of an
2 uncertainty factor.

3 PANEL MEMBER BLANC: Right.

4 And the other reason why I think it's kind of
5 critically important that perhaps that be pretty explicit
6 in the document is because apparently federal EPA has
7 opted not to use a safety factor in their Endosulfan risk
8 assessment, if I understand correctly.

9 CHAIRPERSON FROINES: That is currently being
10 considered at this point. And they had proposed -- and
11 their rationale for going to a one safety factor -- no
12 safety factor was, in my view, slightly bizarre, and I
13 won't go further, but it was very contradictory. So I
14 don't know how it's going to turn out. But they're going
15 to be under a lot of pressure to not stay with that
16 position I think.

17 PANEL MEMBER HAMMOND: I'd like to state one of
18 my view points on the question of childhood safety factor.

19 We --

20 CHAIRPERSON FROINES: Thanks, Melanie and George.

21 PANEL MEMBER HAMMOND: I think that that's an
22 issue that we will probably need to be pursuing in the
23 future and will simply be part of what we'll be looking at
24 in the non-cancer risk assessment methods. And so these
25 are new issues that we're looking at. They have the new

1 legislative mandates that the SRP is facing. I think
2 they're very important issues. They perhaps increase
3 sensitivity of children.

4 I think there -- even without having resolved
5 those issues though, we can actually take other pieces of
6 information. And I would say that there have been some
7 testimonies that would indicate that you have to have
8 experimental data proving greater sensitivity of young
9 animals than adult animals in order to think that there's
10 an age effect.

11 However, I think we do know enough toxicology
12 that for certain systems such as neurotoxicology, we know
13 that in general since the systems aren't fully developed
14 that they tend to be more sensitive. And so we can
15 without knowing what the safety factor is be aware that we
16 would expect even without animal data that there would be
17 more sensitivity of young humans than for adults. And so
18 I think we can actually look at that. That's part of the
19 science basis that we already have.

20 So I think the question of what level of evidence
21 is needed, do we need it in this -- I would think at that
22 point you would almost have to show that there's actually
23 no difference between children and animals. But in the
24 absence of data, I think one would assume that there's a
25 difference.

1 CHAIRPERSON FROINES: Joe.

2 PANEL MEMBER LANDOLPH: Yeah, I was just
3 rereading a document on the way up again. And I realized
4 that there actually is data in here on page 39 that
5 Endosulfan does cause tumor promotion in the hepatocyte
6 foci bioassay. So that statement could be strengthened.

7 The other thing, that I puzzled by the gentox
8 data, because some's positive and some assays don't work.
9 And it turns out earlier in the document they indicated
10 that Endosulfan can generate reactive oxygen species and
11 they have an unusual and unique gentox profile. So that
12 would rationalize some of this data. We'll probably put
13 that in the findings too. Then we'll shortened it.

14 CHAIRPERSON FROINES: Do you have a reference on
15 reactive oxygen species?

16 PANEL MEMBER LANDOLPH: They do.

17 CHAIRPERSON FROINES: They do?

18 PANEL MEMBER LANDOLPH: It's called Soan, et al.,
19 2004. And they're looking in *Saccharomyces Cerevisiae*.

20 CHAIRPERSON FROINES: And do you know what they
21 used as their endpoint?

22 PANEL MEMBER LANDOLPH: TBARS, thiobarbituric
23 acid reactive substances, looking at lipid proxidation.
24 And I'd have to pull a paper to get more detail on it.

25 CHAIRPERSON FROINES: Well, you know, there's

1 that big fat double bond that nobody's talked about yet
2 that's going to potentially epoxidize and then form diols
3 and -- and so that there are pathways that one could think
4 would lead to reactive oxygen species. So that I've
5 thought about that and just decided not to bring it up,
6 because we've had enough complexity anyway.

7 But, I think that -- my feeling is the metabolism
8 as we know it thus far is probably incomplete and that
9 there are probably other metabolic pathways that could
10 lead to other forms of toxicity.

11 PANEL MEMBER LANDOLPH: And the reason I brought
12 that up was I was looking at the gentox profile again and
13 it was a little -- it was interesting. And you get more
14 chromosome breakage and less mutation. And that's true
15 with oxygen radical species, because the assays don't
16 detect their activity very well. So it's a consistent
17 pattern.

18 CHAIRPERSON FROINES: Those are rigid molecules
19 though, those more bornal structures. So it's not quite
20 as simple as I just made it. But it's something that it
21 would be nice to see some experimental data, you're
22 not -- because I don't think they missed it. I think it
23 isn't there. Don't you think?

24 PANEL MEMBER PLOPPER: Um-hmm. That's what I
25 think.

1 CHAIRPERSON FROINES: Yeah, I think Charles and I
2 would be on the same page on this one.

3 PANEL MEMBER HAMMOND: I have a comment about the
4 findings, and just in their -- I actually tried fairly
5 unsuccessfully to get some guidance on the findings and
6 just what should be in them. I understood Gary wanted
7 short findings. But I've also been unclear -- and I don't
8 know whether this is a conversation to have here or
9 elsewhere -- how much the findings need to contain within
10 themselves the data or how much we just say that the data
11 are in the report and we just make up, you know, like --
12 how would it be to say that there is evidence that
13 endotoxin is a tumor promoter, period? Would that be a
14 finding? Would that be sufficient?

15 PANEL MEMBER FRIEDMAN: I would be in favor of
16 that. In fact, I would suggest that you read -- that
17 Kathy be provided with some of our previous findings, that
18 you're relatively new -- you know, if you could see what
19 we've done before with some of the other chemicals.

20 PANEL MEMBER HAMMOND: But you would consider
21 that a sufficient finding?

22 PANEL MEMBER FRIEDMAN: I would think that would
23 be sufficient.

24 PANEL MEMBER HAMMOND: And would other members of
25 the Panel feel that way?

1 PANEL MEMBER BLANC: I think it depends on --
2 obviously it depends on the spin that's in the document.
3 If in fact what you're saying --

4 PANEL MEMBER HAMMOND: I think that's part of the
5 problem.

6 PANEL MEMBER BLANC: Right.

7 PANEL MEMBER HAMMOND: That's the problem that
8 we've been --

9 PANEL MEMBER BLANC: Right. So I think what you
10 want to do is choose the things. So on the things in
11 which there doesn't seem to be any heterogeneity of views
12 and the data are straightforward, I don't think you need
13 to -- we provide the detail. So, for example -- just a
14 quick example, point number one, which is, you know, a
15 full paragraph, I mean basically I think that can be two
16 sentences because I don't think you need to recapitulate
17 that. But if you're going to have a finding that more
18 strongly emphasizes the potential tumor promoter potential
19 of the compound which was only alluded to in passing in
20 the document, then I think it's worthy to say although it
21 was not strongly emphasized in the document, you know, we
22 believe there was convincing evidence to suggest it was a
23 blah, blah, blah.

24 CHAIRPERSON FROINES: Well, I have a question for
25 people. Let's assume that we want to say Endosulfan is a

1 tumor promoter and so Joe wants to know if that's
2 sufficient. One could say that the evidentiary basis is
3 sufficient to conclude that Endosulfan is a tumor promoter
4 and then put page numbers in parentheses where the actual
5 evidentiary basis is found in the document.

6 What do you think of that?

7 PANEL MEMBER FRIEDMAN: That would be great.

8 CHAIRPERSON FROINES: That way you have your
9 evidentiary basis but you don't have -- but you haven't
10 said it in a million -- at length.

11 Paul

12 PANEL MEMBER BLANC: Again, I think it depends on
13 the point you're trying to make. So, for example, this
14 discussion we just had with Melanie about an article which
15 doesn't appear in the report because it has only just now
16 been published. I think that would require obviously more
17 detail describing that publication should we -- should you
18 choose to invoke --

19 CHAIRPERSON FROINES: Well, I don't know what the
20 rules are. Can we in our findings put something in that's
21 not in the record?

22 PANEL MEMBER BLANC: We can --

23 PANEL MEMBER HAMMOND: You mean not in the
24 report?

25 PANEL MEMBER BLANC: I think we just put it in

1 context.

2 CHAIRPERSON FROINES: No, I mean the record. The
3 record -- we could --

4 PANEL MEMBER HAMMOND: It could be in the record
5 if we talked about it in here.

6 CHAIRPERSON FROINES: The record of the whole --

7 PANEL MEMBER BLANC: It's in the record because
8 OEHHA's put it in their findings. So we were supposed to
9 review OEHHA's findings too. So I don't see any problem
10 with that. It's not something I found on med line.

11 PANEL MEMBER BYUS: I have now read the draft
12 findings. I think they're an excellent first draft. I
13 think they're -- it's got all the information in there.
14 Now, all you have to do is edit it down. Take another
15 view of it and make your points. I mean I think you
16 made -- it's an excellent first draft for findings. So
17 just edit them down. And whether it's two pages or four
18 or six pages or however many it is -- I mean I think
19 you're just speaking about tumor promoter. I think you've
20 summarized the data quite nicely and made the right sorts
21 of value judgments and conclusions.

22 So, again, you want to have it longer, a little
23 shorter, I think is what you should do. So I think it's
24 an excellent first draft for --

25 CHAIRPERSON FROINES: I still maintain that the

1 context or the purpose of findings is to describe the
2 basis for your decision. And everything else is in the
3 document.

4 PANEL MEMBER BYUS: And what they've done is
5 pulled out of the document all of those key
6 findings -- the key aspects and summarized them here in
7 their first draft. So that's the decision. Do you want
8 to leave them here or refer to them back in the document?
9 But in your thinking, your thinking is all done. It's
10 just a matter of where you put it as far as I could -- as
11 I read.

12 CHAIRPERSON FROINES: Well, but you agree with
13 Gary as well.

14 PANEL MEMBER BYUS: Um-hmm. I think it should be
15 tightened up. I mean it's a first draft. So, yes. And
16 so you've got all your -- the way I read this, you've
17 pulled all of the document, all of the key aspects,
18 reiterated them. So that your conclusions at the end of
19 every paragraph were supported by the document and your
20 thinking. So I mean it's just a matter of deciding to
21 reference back into the document or leave them here in the
22 findings.

23 CHAIRPERSON FROINES: You know what's clear about
24 this discussion? Is that we are academics.

25 (Laughter.)

1 CHAIRPERSON FROINES: Only academics can take a
2 topic and after a hundred meetings haven't resolved it
3 yet.

4 (Laughter.)

5 PANEL MEMBER BYUS: If you read what they've
6 said, I mean they've made some very -- they've made all
7 the right value judgments as far as I can see. And it's
8 here.

9 CHAIRPERSON FROINES: Now, the point is that as
10 they and then me are working on them, what we would
11 prefer -- what we would want of course is Emails to, say,
12 Joe or -- say Joe just for the sake argument -- that if
13 you have input, don't just wash your hands of it after --
14 in the next five minutes.

15 What?

16 PANEL MEMBER BLANC: Nothing.

17 PANEL MEMBER LANDOLPH: Mechanistically I think
18 what might work is let Kathy and I take another crack at
19 it from the electronic copy we gave to Jim, and let us
20 work to shorten it. And then we'll send it to you and you
21 send it to the whole committee. You want to do that? And
22 then just send us back any comments you have and we'll be
23 happy to put them in.

24 CHAIRPERSON FROINES: I really want to come into
25 the next meeting with being able to start and take a vote.

1 Hopefully we can eliminate lengthy discussions.

2 PANEL MEMBER FRIEDMAN: But we'll get a chance to
3 see it before the meeting, right?

4 CHAIRPERSON FROINES: You'll have multiple
5 opportunities. It's embarrassing, frankly, that you
6 didn't have it until this morning.

7 PANEL MEMBER BLANC: You know, Joe, I want to
8 suggest a slight modification of that, because it's -- you
9 guys have worked so hard on it and it's really, you know,
10 hard to take a step back. I really would suggest that
11 John do a big, big trimming and send it back to you guys
12 for your vetting as the next step.

13 PANEL MEMBER LANDOLPH: That's fine. But I'd
14 like to do just a few more things before he does that.

15 (Laughter.)

16 CHAIRPERSON FROINES: This is my friend Paul
17 Blanc.

18 (Laughter.)

19 PANEL MEMBER LANDOLPH: I know that.

20 CHAIRPERSON FROINES: Yeah, I think -- I agree.
21 I actually think that having a fresh face to work on it --
22 I think Paul's right, that I think I can bring a fresher
23 face than you two can.

24 PANEL MEMBER BLANC: And, believe me, it's been a
25 number of years since John was referring to as a fresh

1 face.

2 (Laughter.)

3 CHAIRPERSON FROINES: So are we done for this --
4 at this point we're beginning to drag it out.

5 PANEL MEMBER BLANC: Yeah. No, fine. I think we
6 know what we're doing.

7 CHAIRPERSON FROINES: So let's take a ten-minute
8 break and then start with OEHHA.

9 (Thereupon a recess was taken.)

10 CHAIRPERSON FROINES: We are starting with OEHHA.

11 And it is my understanding, Andy, that today
12 you're making a presentation and then we're going to
13 discuss it at the next meeting and that you're not
14 anticipating a lot of feedback today. But is there any
15 reason why we couldn't give you feedback if we wanted to?

16 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF
17 MARTY: No.

18 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
19 CHIEF SALMON: I'll hand over to Melanie here. She was
20 going to introduce the topic, so she can explain best.

21 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF
22 MARTY: That's correct.

23 No, we'd be happy to take feedback at any point,
24 today included.

25 I did want to just reiterate for the record that

1 we extended the public comment period upon request from a
2 number of people. And so that threw us off a little bit
3 timing-wise. So the Panel has only received the public
4 review draft of the document. And we are going to give an
5 introductory presentation today and answer whatever
6 questions we can answer.

7 But we aren't going to go through the individual
8 chemical RELs today and we're not going to -- obviously
9 can't go through the public comment. The public comment
10 period ended three weeks ago. So we have the comments now
11 and we're going to be in the process of responding to
12 them.

13 The normal process is you guys get the document,
14 the comments, and our responses all at the same time. So
15 it just got a little bit split this time.

16 So, yes.

17 CHAIRPERSON FROINES: When will the -- the
18 document I notice was missing was Appendix D.

19 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
20 CHIEF SALMON: No.

21 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

22 MARTY: Appendix D was the individual reference exposure
23 levels for the six -- I think we had six chemicals.

24 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
25 CHIEF SALMON: Yes.

1 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

2 MARTY: So --

3 CHAIRPERSON FROINES: They weren't in my package.

4 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

5 CHIEF SALMON: I think we sent -- I think I -- I Emailed
6 you them separately, I think, didn't I? But, in fact,
7 what -- I think what happened is you were expecting all of
8 the RELs in Appendix D. That's not what you're getting.
9 What you're getting doesn't -- by design, doesn't include
10 the existing RELs. It only includes the six new ones. So
11 the Appendix D, as you have it, and as you will have it
12 for the purposes of review, consists of the six new REL
13 summaries. It doesn't include -- you know, when it's
14 final, we would add in the existing RELs which have not
15 been changed from the old document. Does that make sense?

16 CHAIRPERSON FROINES: Yep.

17 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

18 MARTY: Okay.

19 CHAIRPERSON FROINES: At the risk of getting
20 people to laugh, you noticed why I noticed that I was
21 missing appendix D right away. Because that's the
22 appendix that has naphthalene in it and --

23 (Laughter.)

24 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

25 CHIEF SALMON: Yes. Well, naphthalene is not one of the

1 first six. But it will be coming along obviously as an
2 existing REL until such time as it's updated, which I
3 think is likely to happen in the --

4 CHAIRPERSON FROINES: You realize that you have
5 both Dr. Plopper and me on the naphthalene thing, so that
6 that's the one you have to be really be careful about it.

7 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
8 CHIEF SALMON: Well, that's why we didn't include it in
9 the first six.

10 (Laughter.)

11 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF
12 MARTY: That was a joke, by the way.

13 Okay. I'm going to turn it over to Andy, and he
14 will make the presentation.

15 (Thereupon an overhead presentation was
16 Presented as follows.)

17 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
18 CHIEF SALMON: Okay. Now what I say actually I mean.

19 (Laughter.)

20 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

21 CHIEF SALMON: Okay. So I'm Andy Salmon. I'm with the
22 Office of Environmental Health Hazard Assessment. And I'm
23 going to move the microphone closer so you can hear me.

24 So this presentation is a summary of what we've
25 been doing with this revised non-cancer risk assessment

1 methodology document. And I'll just start -- what I'm
2 going to do is I'm going to basically concentrate on what
3 has changed from the previous go-around. So some of
4 the -- some of you will in fact recall the process by
5 which we generated the original air toxics hot spots.

6 CHAIRPERSON FROINES: Can I ask a question?

7 Is there anybody here from DPR?

8 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

9 MARTY: Lori.

10 CHAIRPERSON FROINES: Oh, so there are people
11 from DPR? I just couldn't see around people's heads. I
12 just wanted to make sure, because obviously some of the
13 issues that came up in Endosulfan are going to come up
14 right now. And so I wanted to make sure that there was
15 communication going back and forth.

16 Go ahead, Andy.

17 --o0o--

18 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

19 CHIEF SALMON: Okay. So essentially what has happened is
20 that we have a mandate particularly from the Children's
21 Environmental Health Protection Act, SB 25, to ensure that
22 quantitative risk assessments are child protective. And
23 part of that mandate is to reevaluate the methods for
24 deriving reference exposure levels for non-cancer
25 endpoints. And we are also taking the opportunity to

1 incorporate new scientific developments in risk assessment
2 methodology since it's ten years since we last looked at
3 the methodology documents.

4 --o0o--

5 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

6 CHIEF SALMON: The requirements of SB 25, basically that
7 we take into account any source of difference in response
8 of infants and children, does in fact also mention other
9 sensitive subpopulations. But the emphasis is on infants
10 and children. We need to consider differences in exposure
11 patterns, differences in susceptibility of infants and
12 children to the toxic effects.

13 We're also instructed to take into account the
14 effects of co-exposure to other substances with common
15 mechanisms of toxicity and interactions of multiple air
16 pollutants. There is going to be some general guidance in
17 that area. But unfortunately at this point the science
18 doesn't give us a great deal of opportunity to address
19 those last two issues in detail. But obviously where we
20 do have that opportunity, we'll take it.

21 CHAIRPERSON FROINES: Does the special
22 susceptibility include metabolic differences?

23 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

24 CHIEF SALMON: Absolutely. It includes any source -- as
25 we read the statute, it includes any source of

1 differential impacts, including metabolic differences,
2 physiological differences, and so on, as I will elaborate
3 in due course.

4 --o0o--

5 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

6 CHIEF SALMON: Just by way of background, these guidelines
7 are designed specifically to support the risk assessments
8 undertaken under the Air Toxics Hot Spots Program. It's
9 been mentioned by Dr. Froines, among others, that these
10 guidelines certainly are reflective of how we do things
11 generally and are looked at with interest by other OEHHA
12 programs and other California programs and, indeed,
13 outside of California. But the specific regulatory
14 application of this document is the Air Toxics Hot Spots
15 Program.

16 The previous guidelines to which I referred,
17 basically the Parts 1 to 4 of the technical support
18 document, which was an exercise required by statute that
19 we produce formal guidelines and have them reviewed by the
20 Scientific Review Panel, and these four existing parts are
21 the ones which are currently in force.

22 The acute toxicity dates from 1999 and the
23 chronic toxicity dates from 2000. The exposure -- the
24 cancer potency was 2000 also. And the exposure assessment
25 is somewhat more recent. I think that's about 2003 or

1 something, is it not?

2 CHAIRPERSON FROINES: Is there a document that
3 addresses uncertainty on a quantitative basis and talks
4 about Monte Carlo?

5 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

6 CHIEF SALMON: Some of that appears in Part 4 as regards
7 the exposure assessment and stochastic analysis area.
8 That's where -- some elements of that.

9 Other uncertainty-based considerations also
10 appear in the non-cancer and cancer toxicity technical
11 support documents.

12 --o0o--

13 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

14 CHIEF SALMON: This presentation in this document refer to
15 risk assessment for non-cancer toxicity. And in
16 attempting to update the methodology for the reference
17 exposure levels, we decided that the old guidelines -- we
18 had two separate documents, one for acute and one for
19 chronic. And we felt that the reasons and justifications
20 for that were in fact largely historical, and that it
21 would make more sense for this revision to tackle both
22 acute and chronic toxicity in the same non-cancer toxicity
23 document. So this proposed document, which you have in
24 front of you, is designed to replace Part 1 and Part 3 of
25 the existing TSD series.

1 applied are situations where access by children is
2 actually statutorily limited. It's like some work places.
3 Whereas, other cases we do want to have children included
4 in the population and consideration.

5 PANEL MEMBER BLANC: Andy, what is an off-site
6 worker?

7 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
8 CHIEF SALMON: If you have a -- well, a typical hot spots
9 emission site is, you know, a factory of some kind. And
10 if that is in, say, you know, an industrial park and
11 there's another factory next door to it and it happens
12 that your maximally exposed individual which you're using
13 the base of your risk assessment is actually a worker in
14 that second factory, that's an example of an off-site
15 worker type of situation.

16 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF
17 MARTY: Just remember that these numbers are used in risk
18 assessments of specific stationary sources. And so the
19 requirements are to look at the dispersion of the air
20 pollutant into the surrounding area. Sometimes a
21 surrounding area is not residential. It's office
22 buildings or another facility. And so the impacts are
23 really to people who happen to be there eight hours a day
24 off-site.

25 We don't deal with on-site workers, because then

1 we're stepping on Cal OSHA's toes. And that's why we call
2 them the off-site workers. They're the ones that have the
3 impact from the plume of whatever facility that is being
4 evaluated.

5 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

6 CHIEF SALMON: I'll also interpose a comment here about
7 this area, that obviously you're going to be hearing a
8 great deal more about this sort of application of not only
9 the eight-hour REL but the others as well, because you are
10 in due course going to be seeing an update of the Part 4
11 technical support document, the exposure assessment part.
12 And so a lot of the -- you know, the detailed
13 considerations of how the exposure assessment is done, how
14 the target individual or population is defined, and how
15 the RELs are going to be used is actually going to be
16 appearing in that document rather than in this one. This
17 document is going to be just about how we -- how we derive
18 the RELs, and we've set up some definitions of what they
19 are in the document. But we don't in this document cover
20 how they're going to be applied in any detail.

21 --o0o--

22 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

23 CHIEF SALMON: Excuse me. That was supposed to
24 go -- okay.

25 Why am I going backwards? Sorry. It's all a

1 question of clicking the right button.

2 Another change in general guidance principles is
3 in relation to the use of uncertainty factors. I've
4 already mentioned this concept that we would be replacing
5 the uncertainty factors by models. And part of the way
6 that the people have been thinking about these uncertainty
7 factors in the published literature, particularly over the
8 last 10 or 15 years, is that the inter- and intraspecies
9 uncertainty factors, which previously were more or less
10 just seen as individual black boxes with a value of 10,
11 people have been thinking about those as composed of two
12 separate components: A pharmacokinetic component, in
13 other words an area of uncertainty which addresses
14 differences in absorption, metabolism, distribution,
15 excretion and that part of the process; and then a
16 pharmacodynamic or toxicodynamic component, which is
17 actually differences or uncertainties in the response of a
18 target individual.

19 And the way people have addressed these areas of
20 uncertainty in extrapolating both between species and
21 between individuals within a species has been to use
22 models where they're available. We may well have a
23 pharmacokinetic model but not a pharmacodynamic model. So
24 it's convenient to separate out these uncertainty factors
25 into these two subcomponents. And there's been a

1 considerable difference -- well, there's been a
2 considerable discussion of this in the scientific
3 literature. I'm not -- you know, I don't want you to
4 think we invented this. But we've read it and we think
5 it's useful.

6 --o0o--

7 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
8 CHIEF SALMON: Another change in general guidance
9 principles is the use of benchmark concentration
10 methodology where data permit. You have in fact seen this
11 in several recent REL determinations which you considered.

12 It was mentioned as a possibility in the previous
13 guidelines, but has been much more thoroughly developed in
14 recent years.

15 And the benchmark concentration method is now, in
16 fact, in our view, preferred wherever possible rather than
17 the more traditional NOAEL/LOAEL method.

18 PANEL MEMBER FRIEDMAN: Would you mind explaining
19 why that is preferred? Or would you rather wait till
20 after your presentation?

21 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
22 CHIEF SALMON: I can explain now briefly. I mean
23 essentially it's a statistical argument in that the
24 benchmark methodology looks at all the --

25 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

1 MARTY: The next slide is a good thing to look at.

2 There you go.

3 --o0o--

4 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

5 CHIEF SALMON: The method actually looks at all the data
6 which you have. It looks at all the exposure levels. And
7 taking that into account obviously produces a more robust
8 result in statistical terms than just looking at the
9 single point of the low end of the curve, which is what
10 you're looking at when you're trying to find out what the
11 NOAEL is. That's the essence of it.

12 It uses -- also it uses statistical curve fitting
13 methodology to estimate the overall dose response curve,
14 rather than just taking a single value. So it actually
15 allows you to calculate confidence bounds. And so -- I
16 mean you know the uncertainties there. But this gives you
17 some measure of at least part -- the size of what that
18 uncertainty is.

19 So I think that's in a nutshell why it's
20 preferable. It certainly has properties of providing
21 better independence of the actual study design and exactly
22 where the dose levels were selected and things like that
23 as well.

24 PANEL MEMBER FRIEDMAN: But if I understand it
25 correctly, you select the dose that causes an effect in 5

1 percent of the subjects?

2 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

3 CHIEF SALMON: Yes, we do.

4 PANEL MEMBER FRIEDMAN: So that's really not a
5 "no effect"?

6 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

7 CHIEF SALMON: Well, in fact, it is, in the sense that
8 what you call a "no effect" -- remember, in the
9 traditional method it's called a "no observable adverse
10 effect level." And what you're actually saying is that --
11 you know, what you select as the NOAEL is the level at
12 which you can no longer observe any effect. And if you
13 look at the actual size of the studies and their
14 statistical power, what you actually find is that if you
15 had a response rate which was less than something around 5
16 percent, then you wouldn't see it unless you were very
17 lucky. So in fact -- yeah, for a typical animal study.

18 We've actually done quite a number of these
19 benchmark dose estimations now and we've compared what we
20 would get using the benchmark dose methodology and
21 selecting a -- it's the lower confidence bound on the ED05
22 is the proposed benchmark. And if we look at what we get
23 by that method and then compare it to what we get by the
24 more traditional NOAEL method, where we can determine a
25 NOAEL, the NOAEL and the LED05 look very similar in the

1 majority of cases where we're looking at standard animal
2 studies which have a quantal endpoint.

3 Now, this recommendation for LED05 does not apply
4 to continuous data, because there are other different
5 statistical considerations for statistical -- for
6 continuous data. It also doesn't apply to analysis of
7 epidemiological studies, because what constitutes an
8 observable effect is a function in that case of the size
9 of the study and the methodology. So those two situations
10 we don't have a generic recommendation. We're saying you
11 just to have look at the study and decide what would be an
12 appropriate benchmark.

13 But for the -- for the quantal study in animals,
14 the standard sort of tox data that you see most of the
15 time, our experience is that the LED05 has similar
16 properties to what is commonly referred to as a NOAEL.

17 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF
18 MARTY: Krewski did an analysis at one point and published
19 it of the NOAEL and where that was on the response
20 fraction. And it's anywhere between 1 and 20 percent for
21 typical animal studies. One percent would be a pretty
22 large animal study. So epidemiologists are used to
23 looking at large numbers of people, and most of the tox
24 data is not large numbers of animals

25 PANEL MEMBER BYUS: For what it's worth, I agree

1 with you.

2 (Laughter.)

3 PANEL MEMBER BYUS: It's the thing to do.

4 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

5 CHIEF SALMON: Well, as I say, we do have some experience
6 with it now, which you have seen several examples of. And
7 on the whole we agree with Krewski and others that this is
8 a more robust method in situations where it can be
9 applied.

10 PANEL MEMBER BYUS: You don't always have the
11 data though. That's the problem.

12 CHAIRPERSON FROINES: Can you make available that
13 reference.

14 I also think that the original Kenny Crump paper
15 is still one of the best papers on this topic. You know,
16 it really lays it out.

17 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

18 CHIEF SALMON: Yes.

19 CHAIRPERSON FROINES: And it deals with quantal
20 and continuous issues.

21 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

22 CHIEF SALMON: Yes. We would be -- yeah, we have I think
23 most of those references. I think all of them.

24 CHAIRPERSON FROINES: Well, that paper is -- it's
25 probably like '83, but it still reads very, very well.

1 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

2 CHIEF SALMON: Yes. Those are cited in the document. But
3 I think we can get copies of those to you if you would
4 like.

5 PANEL MEMBER FRIEDMAN: I would very much
6 appreciate that.

7 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

8 CHIEF SALMON: Yes, certainly, we'll do that.

9 OEHHA DEPUTY DIRECTOR ALEXEEFF: George Alexeeff.

10 There was one other paper by Leisenring and Ryan
11 that also looks at another kind of -- same analysis but
12 sort of different perspective. So I think there's --
13 there's two or three papers that kind of looked at it from
14 a probabilistic approach.

15 CHAIRPERSON FROINES: Well, then there's all the
16 work that Dale Hattis did looking at -- and others looking
17 at this factor of 10 and whether it's adequate or
18 inadequate.

19 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

20 CHIEF SALMON: Yes. I'm going to be talking about that
21 next, or very soon, if you want me to do that.

22 CHAIRPERSON FROINES: No, go ahead.

23 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

24 CHIEF SALMON: Yes. The next area I'm going to talk about
25 is in fact, you know, how the extrapolation is going to

1 work, how we use the uncertainty factors, and what values
2 they should have.

3 First extrapolation to consider is the
4 interspecies extrapolation. And this is traditionally
5 being handled by means of an uncertainty factor of 10 in
6 taking the applied concentration in the test species to an
7 equivalent applied concentration for a human.

8 And this somewhat complicated diagram is
9 basically designed to indicate the stages of the
10 extrapolation, at least conceptually, and the fact that
11 these can in fact be, if necessary, individually replaced
12 by quantitative models. And to the extent that we are
13 able to use quantitative models, we would be replacing the
14 uncertainty factor or some part of it with that model.
15 But we might have to retain some of the uncertainty factor
16 if there were other areas which were not being dealt with.

17 CHAIRPERSON FROINES: Andy, I have a question
18 about that. Because it's one thing -- here's your
19 uncertainty factor over here. And then over here you talk
20 about the pharmacokinetic and pharmacodynamic aspects of
21 models. But the problem is the pharmacodynamic part of
22 that is very difficult and very, very uncertain, it seems
23 to me.

24 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
25 CHIEF SALMON: Yes.

1 CHAIRPERSON FROINES: So you've kind of
2 got -- the danger is that you begin to mix all sorts of
3 things that shouldn't be mixed. You know what I'm saying?

4 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
5 CHIEF SALMON: Well, that's one of the reasons why we
6 tried to separate the two areas conceptually and to think
7 in terms of two separate subfactors rather than an overall
8 interspecies or intraspecies uncertainty factor. And it's
9 also why we amused ourselves generating these complicated
10 pictures, to try and emphasize that these were separate
11 components and that, you know, dealing with one does not
12 deal with the other.

13 And while I would certainly agree -- and I think
14 it may even be in my next slide -- I say --

15 --o0o--

16 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
17 CHIEF SALMON: -- that we're well aware that there are few
18 cases where we have good toxicodynamic models, but we do
19 in fact now have some reasonable toxicokinetic models for
20 certain cases. So this is one of the reasons for our
21 laying out the idea that there are these two separate
22 components of the uncertainty in extrapolation and that
23 dealing with one explicitly does not deal with the other.

24 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF
25 MARTY: I think it's also fair to say that there are cases

1 where the two are petty well intertwined.

2 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

3 CHIEF SALMON: Yes. I mean obviously once you start
4 getting into the area of talking about specific models,
5 then it becomes very case specific and you're responding
6 to what data you actually have and how much you understand
7 of the problem.

8 PANEL MEMBER BYUS: What does the threefold mean
9 there?

10 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

11 CHIEF SALMON: Well, basically that what we're saying here
12 is that the traditional overall value of UFA has been 10.
13 And as a default, for want of better information, we're
14 assuming that the uncertainty represented by the
15 toxicokinetic extrapolation and the uncertainty
16 represented by the toxicodynamic extrapolation are equal
17 in size. Which in the way that the --

18 PANEL MEMBER BYUS: How do you make that
19 assumption?

20 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

21 CHIEF SALMON: Well, because we don't know what else to
22 assume.

23 PANEL MEMBER BYUS: Well, I don't see how you can
24 make that assumption. That's a false assumption.

25 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

1 CHIEF SALMON: Well, there are -- I'll come in a
2 minute -- there are --

3 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

4 MARTY: This is what happens when a bench scientist looks
5 at risk assessment.

6 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

7 CHIEF SALMON: Yeah.

8 (Laughter.)

9 PANEL MEMBER BYUS: Well, I mean I don't -- just
10 to pick the 3 out of air -- I mean I agree with you up to
11 this point, that there are these two components. But
12 depending on what you're talking about, you have no idea
13 whether it's threefold or --

14 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

15 CHIEF SALMON: Well, there have in fact been some
16 objective studies of how big the uncertainty factors need
17 to be. And there is some literature suggesting that the
18 overall traditional value of 10 isn't horribly wrong.

19 PANEL MEMBER BYUS: I'm okay with 10.

20 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

21 CHIEF SALMON: And also there is in fact some literature
22 suggesting that the value of -- actually it's root 10, or
23 3.16 if you want to be picky about it -- there is some --
24 you know, there are some reports in the literature
25 suggesting that that isn't too horrible. But --

1 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

2 MARTY: For the kinetics.

3 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

4 CHIEF SALMON: Yeah, mostly on the kinetics side.

5 But I would agree that these are, you
6 know -- this is an arbitrary default to be used in the
7 absence of data.

8 PANEL MEMBER BLANC: The reason you came up with
9 these numbers is so that if you didn't have either, you'd
10 be back to 10?

11 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

12 CHIEF SALMON: Yes.

13 PANEL MEMBER BLANC: And that's why you're
14 doing --

15 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

16 CHIEF SALMON: That's part of logic, yes.

17 PANEL MEMBER BLANC: It's approximately 3 --

18 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

19 CHIEF SALMON: Yes.

20 PANEL MEMBER BLANC: -- or something greater than
21 3? You're not saying that you're now going to have a
22 maximum default of 9?

23 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

24 CHIEF SALMON: No, we're not. We're actually saying
25 explicitly -- people, both ourselves and the EPA in

1 previous guidance, have rather loosely referred to it as
2 about 3. But in fact if you're doing the -- you know,
3 because there's a multiplicative sum, the way it's used is
4 if you have two of these, quote-unquote, three factors,
5 then it multiplies up to 10. In other words the actual
6 value is the square root of 10, or 3.16, that's the
7 assumption, so that it multiplies up to 10.

8 PANEL MEMBER BLANC: And you said you thought
9 that there was some support for the toxico -- I'm sorry --
10 the toxicokinetic variability between species being
11 something like a threefold --

12 OEHHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
13 CHIEF SALMON: Yes, there is some support for that.

14 PANEL MEMBER BLANC: Because if I had to weigh
15 the two of them, I would have thought that the bigger
16 piece of the uncertainty was in the dynamic piece, where
17 it's not that it's metabolized more slowly or cleared more
18 rapidly, but that there was a mechanism of toxicity that
19 differed between species and that's where the uncertainty
20 was, and it didn't have to do with how much of the -- it
21 wasn't that it was going down a different pathway in
22 humans or something?

23 OEHHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF
24 MARTY: There are most definitely those examples.

25 OEHHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

1 CHIEF SALMON: Yeah, I think the point is that it's
2 definitely -- it's case dependent. You know, there are
3 some cases where the kinetic uncertainty is large, and
4 there are certainly also some cases where the
5 toxicodynamic uncertainty is large. But, you know, these
6 are sort of median values for use when you don't know any
7 better essentially.

8 CHAIRPERSON FROINES: But as much as I understand
9 what Paul just said, I actually would take the opposite
10 view, which is that the heterogeneity within the
11 toxicokinetics can be a very large number.

12 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
13 CHIEF SALMON: Well, I mean I think we're agreeing that
14 you're both right. It depends which sort of -- you know,
15 which compound you're looking at. In some cases that
16 uncertainty, you know, will be biased in one direction, in
17 other cases it will be biased in the other. But what
18 we're saying here is if you had the information where you
19 could say that, then you would be using that information.
20 Even if you didn't have a good model, you'd be -- if you
21 had information which even if it didn't give you a
22 quantitative model, allowed you to say that "in this case
23 I think the toxicodynamic uncertainty should be 10," then
24 you would do that.

25 PANEL MEMBER BYUS: I guess I'm -- I think

1 everything you're saying is reasonable.

2 But let's assume you had the data -- I mean I'm
3 just confused. Let's assume you had the data on the
4 toxicokinetic differences in the individual model of the
5 animal and it was fourfold. Now, are you saying --

6 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

7 CHIEF SALMON: You'd use 4.

8 PANEL MEMBER BYUS: Okay. But then you would not
9 use the 10X?

10 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

11 CHIEF SALMON: No, if --

12 PANEL MEMBER BYUS: You'd only use the 4?

13 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

14 CHIEF SALMON: Well, if --

15 PANEL MEMBER BYUS: And then you would pick this
16 other one as the default 3 for the pharmacodynamic, is
17 that what you're saying?

18 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

19 CHIEF SALMON: Yeah, if we had -- in any case if we have
20 real data, we would be using the real data rather than the
21 default.

22 PANEL MEMBER BYUS: If you only -- what I'm
23 asking you is if you only have half of the real data -- in
24 lieu of the tenfold uncertainty factor, say, you only have
25 the toxicodynamic -- or toxicokinetic data or you have the

1 toxicodynamic -- I don't care which one --

2 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

3 CHIEF SALMON: Yeah. We would be using the -- but we are
4 viewing those separately. So if we had the one but not
5 the other --

6 PANEL MEMBER BYUS: So my question is: What do
7 you do with the missing one? How do you apply it?

8 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

9 MARTY: We're getting to that.

10 PANEL MEMBER BYUS: What is the value applied to
11 the missing one?

12 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

13 MARTY: We would have -- we're getting to that. In the
14 next few slides you'll see that.

15 But we would not just replace the toxicodynamic
16 uncertainty factor, because we knew something about the
17 toxicokinetics.

18 PANEL MEMBER BYUS: That's what I'm saying. If
19 you know something about the toxicokinetic and don't know
20 anything at all about the toxicodynamic, what do you do?

21 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

22 CHIEF SALMON: Well, we'd use what we know to determine an
23 appropriate value for a toxicokinetic factor and we'd use
24 the default for the toxicodynamic, because we don't
25 have --

1 PANEL MEMBER BYUS: And that number is?

2 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

3 MARTY: Root 10,

4 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

5 CHIEF SALMON: Root 10.

6 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

7 MARTY: About 3.

8 PANEL MEMBER BYUS: It's 3?

9 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

10 MARTY: Yeah.

11 PANEL MEMBER BLANC: 3.1 something.

12 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

13 CHIEF SALMON: 3.16.

14 PANEL MEMBER BYUS: And so say the toxicokinetic

15 factor was 1.5X. So you would be using -- and so you

16 would use 3 for the toxicodynamic --

17 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

18 CHIEF SALMON: Yes.

19 PANEL MEMBER BYUS: -- and that would be less

20 than the 10?

21 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

22 CHIEF SALMON: Yes.

23 PANEL MEMBER BLANC: But it could be more than

24 10?

25 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

1 MARTY: It could be more than 10.

2 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

3 CHIEF SALMON: It could equally well be more than 10.

4 PANEL MEMBER BLANC: Right, because if they had a
5 value of 6 that they were pretty firm on for one --

6 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

7 CHIEF SALMON: They are in fact -- although we're not
8 going to be able to get to the discussion of the
9 individual RELs today, you will see examples within that
10 where based on at least partial compound-specific data or
11 mechanism-specific data, we have chosen non-default values
12 for these subfactors. But we do so independently. If we
13 know one, we use the known version. If we don't know the
14 other, then we use the default.

15 PANEL MEMBER BYUS: Well, let me -- and I'll just
16 ask this one last question.

17 So if you -- say the toxicokinetic factor was
18 measured and it was .5, and then you would use 3 for the
19 toxicodynamic, and that would be considerably less than
20 the 10.

21 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

22 CHIEF SALMON: Yes.

23 PANEL MEMBER BYUS: And I'm asking you: Is that
24 in fact the way to do it?

25 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

1 CHIEF SALMON: Well, there's a very slight
2 caveat -- there's a very slight point here, in that at
3 least somewhere in the sort of the depths of our
4 methodology -- I don't think we even necessarily lay it
5 out in the guidelines explicitly. But there's a
6 reluctance to use uncertainty factors of less than 1. But
7 with that caveat, basically -- as I say, if we've got
8 data, we use it; if we haven't got data, we use the
9 default. That's the principle across the board.

10 PANEL MEMBER BYUS: I know, but the -- all right.

11 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

12 MARTY: We'll have a little more discussion time because
13 we're going to get into this same issue for the
14 intraspecies extrapolation. So --

15 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

16 CHIEF SALMON: So if you knew that toxicokinetics was 1
17 and you didn't know anything about toxicodynamics, then
18 you would use a toxicokinetic factor of 1 and a
19 toxicodynamic factor of root 10. And this is in fact, as
20 I'll show -- it may even be the next -- yes it is the next
21 slide.

22 --o0o--

23 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

24 CHIEF SALMON: This is actually what we've been doing all
25 along in one particular case. But I'm going to actually

1 propose a modification of that case. But the point is,
2 that is exactly what we've been doing all along in this
3 particular case.

4 And the particular case is this so-called human
5 equivalent concentration calculation, which we had in
6 the old chronic guidelines. It's a methodology which was
7 developed by U.S. EPA which considers basically deposition
8 in the respiratory tract and uses the areas of various
9 parts of the respiratory tract as a way of estimating what
10 they thought would be the deposition of gases and vapors
11 on the one hand or particles on the other in the various
12 parts of the respiratory tract, and adjusts the equivalent
13 concentration depending on where -- either in the
14 respiratory tract or systemically the toxic effect is
15 appearing.

16 So this is an established method developed by
17 U.S. EPA. We used it previously for the chronic RELs.
18 And it covers deposition. But I'd emphasize, it appears
19 not to have any specific allowance for metabolism or
20 elimination.

21 What we did in the chronic -- old chronic
22 guidelines is where we had one of these calculations, we
23 eliminated the interspecies toxicokinetic factor. We
24 use -- and we'll change it down to 1. So we just used an
25 interspecies factor of 3, which was representing the

1 remaining toxicodynamic uncertainty.

2 However, we have looked at this --

3 PANEL MEMBER BYUS: That's less than the tenfold?

4 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

5 CHIEF SALMON: Yes, it is. It's 3 rather than -- or 3.16

6 rather --

7 PANEL MEMBER BYUS: The total was less than

8 tenfold?

9 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

10 CHIEF SALMON: Yes, the total is less than tenfold.

11 But we looked at this again, and we decided that
12 because this doesn't cover metabolism and all those sorts
13 of processes, that we would not in factor reduce the
14 kinetic uncertainty factor to 1; we'd only reduce it to 2,
15 because we felt that there was still some residual
16 uncertainty due to the metabolism and elimination
17 processes.

18 PANEL MEMBER BYUS: Which are the major
19 considerations by far of the effective dose. I mean
20 disposition is relatively minor, in general. In terms of
21 drugs, it's relatively minor in an effective dose.

22 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

23 MARTY: It is. But I think what you need to think
24 about --

25 PANEL MEMBER BYUS: Yeah, elimination and

1 metabolism are by far the major contribution.

2 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

3 CHIEF SALMON: Well, remember, we're talking about
4 inhalation here. So, in fact, deposition processes can be
5 rather significant, especially when you start talking
6 about particles.

7 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

8 MARTY: So you're going from a rat's snout to a human. So
9 that -- remember, this is going from an animal inhalation
10 exposure to a human equivalent inhalation exposure. So
11 the morphometric differences in the respiratory tract make
12 a fair amount of difference in the dose you actually get.
13 So that was the --

14 PANEL MEMBER BYUS: Right, inhalation, I'm
15 thinking --

16 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

17 MARTY: Yeah, that was the point of this. And we used to
18 just do what EPA did and just say, okay, that takes care
19 of the toxicokinetic differences. But that clearly isn't
20 the case.

21 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

22 CHIEF SALMON: So it's the change in response to the
23 availability of an HEC calculation, which is -- you know,
24 which what is new.

25 So, anyway, but that also -- that also

1 illustrates your point, that, yes, the overall factor in
2 this case would be reduced from 10 to 6 if we still knew
3 nothing about the toxicodynamics.

4 PANEL MEMBER FRIEDMAN: That last part you said
5 you didn't -- you prefer the PBK -- I'm sorry --

6 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
7 CHIEF SALMON: Yes, PBPK model. If we have -- there are
8 now some actually much more complicated kinetic models
9 which consider not only deposition but also metabolism and
10 distribution or at least delivery -- yeah, and
11 excretion -- or at least delivery to a specific site
12 within the respiratory tract, where the effect is
13 occurring. And then you know how that is -- that local
14 concentration response. And there are a couple of
15 examples. Again, you will in fact see an example of the
16 use of such a model in one of the example RELs when you
17 get to looking at that. That's one of the reasons why the
18 example RELs are there hopefully to, you know, illustrate
19 what we're talking about.

20 PANEL MEMBER FRIEDMAN: Does that replace the
21 3.16?

22 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
23 CHIEF SALMON: Well, that would replace -- that model
24 replaces the 3.16, yes.

25 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

1 MARTY: I think it's safe to say though that we're still
2 using uncertainty factors for the majority of chemicals
3 because we lack the models.

4 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

5 CHIEF SALMON: Yes. There are not going to be a lot of
6 situations where we can do that. But where we can, we
7 will.

8 PANEL MEMBER FRIEDMAN: So if 10 milligrams per
9 kilogram causes some effect in a mouse, and you didn't
10 have any of these models to transfer -- you say that you'd
11 assume that the same thing happens for 1 milligram per
12 kilogram in a human?

13 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

14 CHIEF SALMON: That's the underlying assumption, yes.

15 PANEL MEMBER FRIEDMAN: And if it's a dog, it's
16 still 10 to 1, and if it's a rat --

17 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

18 CHIEF SALMON: The guidance as we had it previously and as
19 it continues is that it would be 10 for non-primate
20 species and 3 for primate species.

21 PANEL MEMBER FRIEDMAN: But no matter what the
22 species is?

23 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

24 CHIEF SALMON: Yes.

25 CHAIRPERSON FROINES: Now, we're doing a lot of

1 work on interactions. And it's so strange to sit here and
2 listen to this discussion, because when you start dealing
3 with more than one chemical at a time, this is just
4 bizarre. I mean it's like another -- it's like another
5 world. I mean it's so complex that --

6 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
7 CHIEF SALMON: Well, where we have an interaction
8 situation to deal with, we will be looking forward to your
9 guidance in that regard.

10 CHAIRPERSON FROINES: Well, it's clearly
11 necessary, because, you know, since we have globalization,
12 we don't have any factories anymore, and so we need
13 multiple exposure methods.

14 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
15 CHIEF SALMON: I would certainly agree with that.

16 CHAIRPERSON FROINES: That was a joke.

17 (Laughter.)

18 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
19 CHIEF SALMON: But I'd still agree with it.

20 (Laughter.)

21 --o0o--

22 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
23 CHIEF SALMON: The next one I want to talk about is the
24 question of how do we handle the extrapolation within the
25 human species. And here we're talking about the

1 extrapolating from the average human to either a specific
2 sub-population or a specific individual or a type of
3 individual. And the way this has been done in the past
4 has again been to use an uncertainty factor of 10. But in
5 the similar way to what you've just seen, we're proposing
6 basically to subdivide the extrapolation conceptually into
7 various subparts and that we would again be able to use
8 models to replace either and/or the toxicokinetic and
9 toxicodynamic parts with models. And, again, we're
10 hopeful of having dynamic -- toxicodynamic models but
11 seldom do. But we actually do in some cases have workable
12 pharmacokinetic models.

13 The interesting point here of course, that there
14 are a number of specific individuals or individual types
15 that we would need to consider. But overwhelmingly what
16 we find in practice is that we need to think specifically
17 about children and especially infants, who of course both
18 in overall size and also in physiology and biochemistry
19 are probably most different from adults.

20 --o0o--

21 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
22 CHIEF SALMON: Now, the other question is, when we don't
23 have a model, what do we do? And obviously we're going to
24 have to use the uncertainty factor approach. And as I
25 mentioned, the traditional default has been a UFH of 10

1 composed of two equal factors, one dealing with
2 toxicokinetics and one with toxicodynamics.

3 --o0o--

4 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

5 CHIEF SALMON: Now, we have to consider infants and
6 children. And this slide is an illustration of the truism
7 that children are not -- they're not just small adults.
8 They have considerable differences in anatomy, physiology.
9 There are differences in particularly exposures like
10 respiratory rate, dermal uptake due to both higher surface
11 area and greater permeability. There are differences in
12 excretion. There are physiological differences in body
13 composition like body water and body fat content, which
14 affect how things distribute. And there are different
15 organ system sizes and blood flow, other flux terms likely
16 gastric emptying. And of course, importantly, there are
17 substantial differences in metabolism.

18 PANEL MEMBER BYUS: Let's back up.

19 You might add on that chart incomplete blood
20 brain barrier for infants.

21 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

22 CHIEF SALMON: Absolutely, yes.

23 PANEL MEMBER BYUS: Children often times have
24 higher rates of metabolism for some --

25 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

1 CHIEF SALMON:

2 PANEL MEMBER BYUS: -- particular drugs, not
3 always lower. In fact, it's rather significant in
4 children when they get to be five to ten years old can
5 have actually on a per body weight higher rates of
6 metabolism.

7 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

8 CHIEF SALMON: Yes. And I apologize that this is a
9 summary slide. But, yes, we -- and of course, you know,
10 we've had the opportunity to discuss this with you at some
11 length when we were considering the SB 25 prioritization
12 process. So in terms of what we're going to be doing
13 here, you may consider that everything that we said in
14 that somewhat substantial document is included. And,
15 yeah, you're absolutely right. And of course there are
16 many other specific factors.

17 CHAIRPERSON FROINES: We have found that -- this
18 is a little bit off topic, but let me just ask you about
19 it. We have found that if you have an acute exposure to a
20 reasonable amount of a compound, that very often it
21 disappears very rapidly because of metabolism. But if you
22 have lower dose over a period of time, you actually have
23 more of that compound around to exert toxicity. So that
24 the rate of when we're doing these kinds of experiments
25 for these sorts of purposes, the actual administration of

1 the chemical affects the outcome because the
2 metabolisms -- the metabolisms actually vary. And so
3 that's something that nobody seems to take into account.

4 I can send you some data that I think you'll find
5 interesting.

6 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
7 CHIEF SALMON: Yes. I can envisage situations
8 particularly where, you know, if you had a full PBPK model
9 you would see slower compartments like the less rapid
10 profused organs or the fat and so on. And if you have
11 those slow compartments in the model, then you can have
12 really quite considerable differences between the
13 concentrations achieved at a target organ depending on
14 whether you have a short sharp exposure, which does a sort
15 of quick in, quick out, but mostly via the blood
16 concentration, versus a perhaps lower but longer exposure,
17 which has time to equilibrate the slow compartments.

18 And I'm sure there are other factors as well, but
19 that's certainly possible.

20 CHAIRPERSON FROINES: It's important in air
21 pollution where you have basically constant exposure at
22 low levels. And so you have to ask what's the
23 significance of --

24 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
25 CHIEF SALMON: Well, and that's one; also one of the

1 reasons why we have tended to think somewhat separately
2 about the chronic exposures which reflect ongoing exposure
3 versus the acute one-hour exposures and why -- actually
4 one reason why I think we're asked to look at the
5 eight-hour, because you could argue that, well, you know,
6 in the interests of public health protection just use the
7 chronic all the time and, you know, assume that the
8 eight-hour is going to be like a chronic. But in fact
9 it's not -- you know, it's not as simple as that because
10 of these kinds of considerations.

11 PANEL MEMBER BLANC: Andy, can I just ask, or the
12 Chair, a logistical question. I mean you still have quite
13 a bit of material to go through in terms of the number of
14 slides and how complicated they are.

15 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
16 CHIEF SALMON: Yes.

17 PANEL MEMBER BLANC: It seems to me that if we
18 don't take a brief break now, we're going to really be
19 straining ourselves. I understand that you probably want
20 to break -- you don't want to come back after a lunch
21 break. But I still think we should take some time now.

22 CHAIRPERSON FROINES: My question is: How long
23 do you think you're going to take, given this pace, to
24 finish? And it has to do with whether we think we want
25 lunch or not.

1 My sense is that we're not going to want lunch if
2 there's a -- if we could go a reasonable time, then people
3 could take off. But I don't know what people are
4 thinking.

5 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

6 CHIEF SALMON: I'm about halfway through at this point.

7 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

8 MARTY: Yeah. We can pick up the pace and then --

9 CHAIRPERSON FROINES: So you would say an hour?

10 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

11 MARTY: Oh, yeah. I would say hopefully less than that.

12 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

13 CHIEF SALMON: Yeah, and hope -- well, depending on how

14 many questions you have, of course.

15 PANEL MEMBER BLANC: But he certainly has 45

16 minutes left.

17 CHAIRPERSON FROINES: Well, then we should take a

18 break now.

19 But am I correct that people would prefer to

20 finish rather than take a lunch break if he's got 45

21 minutes?

22 PANEL MEMBER BLANC: I think so. It's the last

23 thing on the agenda.

24 PANEL MEMBER BYUS: Yeah.

25 CHAIRPERSON FROINES: Gary?

1 PANEL MEMBER FRIEDMAN: Sure. I'm hungry, but
2 that's okay.

3 CHAIRPERSON FROINES: Well, you can run
4 downstairs and get a snack.

5 PANEL MEMBER HAMMOND: When is the cake being
6 served?

7 PANEL MEMBER FRIEDMAN: Oh, the cake, right.

8 CHAIRPERSON FROINES: So are we agreed that we're
9 not going to take lunch but we're going to have a break
10 now and then finish off and go our separate ways?

11 PANEL MEMBER BLANC: Yes.

12 CHAIRPERSON FROINES: Okay. Let's take a break.

13 (Thereupon a recess was taken.)

14 CHAIRPERSON FROINES: Do we have a quorum?

15 PANEL MEMBER BLANC: Yes, we do.

16 CHAIRPERSON FROINES: And so, Andy, why don't you
17 proceed.

18 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

19 CHIEF SALMON: Okay. I'll start.

20 So, anyway, we were talking before the break
21 about the intraspecies toxicokinetic extrapolation. The
22 key question is, in view of all these differences between
23 infants, children, and adults, is the traditional
24 toxicokinetic subfactor of 3.16, is that sufficient to
25 protect children as a default? And as we've seen, there

1 are a variety of differences between infants and children
2 and adults.

3 So what we did, we did two things. Firstly, we
4 looked at reports in the literature where there are well
5 described differences in kinetics. And this is mostly in
6 the area of drugs. And we also looked at PBPK modeling,
7 both examples in the literature and also quite an
8 extensive group of studies which we did in-house. Dr.
9 Brown on my staff was a major player on that one.

10 --o0o--

11 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

12 CHIEF SALMON: So the analysis actually suggests that,
13 firstly, there's notably lower clearance or higher --
14 longer half-life of certain drugs in infants. And the
15 PBPK analyses indicate that many chemicals show a larger
16 than threefold variability in either the area under curve
17 or amount metabolized, which are the sort of standard
18 tissue dose kind of measures that you get out of a PBPK
19 model. And so those age differences tend to suggest that
20 threefold may not be enough.

21 --o0o--

22 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

23 CHIEF SALMON: The PBPK modeling we undertook used PBPK
24 models with physiological parameter sets for various ages
25 between newborn and adults. Most of these were -- we

1 didn't necessarily have real infant-specific values for
2 all the physiological parameters. So in many cases, like
3 metabolism, we were forced to use the scaling relative to
4 body weight. But when we did have specific parameters, we
5 tried to use those. And the number of published models
6 were used and looking at metabolites in various target
7 organs.

8 This is obviously to some extent a work in
9 progress, in particular in regard to the need to identify
10 more extensive chemical-specific metabolism data as that
11 becomes available.

12 --o0o--

13 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
14 CHIEF SALMON: But, anyway, the upshot of this is that
15 with a variety of chemicals as the sort of things which
16 are interesting to the Hot Spots Program, certainly in
17 some cases the predicted range of the uncertainty
18 factor -- and this is determined by taking the indicator
19 parameter and looking at the ratio predicted for the adult
20 model versus the infant or child model -- for many
21 compounds admittedly the existing value of 3.16 would be
22 sufficient. But there's a considerable number where it's
23 not. And not quite half of the examples we looked at had
24 something in the range of 3 to 10. And there were several
25 in fact where the number exceeded 10.

1 So I think the first conclusion from this is that
2 the threefold or the 3.16-fold is not sufficient.

3 PANEL MEMBER HAMMOND: Andy, what's the asterisk
4 in that table?

5 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

6 CHIEF SALMON: Yeah, I'm not quite sure. That table was
7 copied from the reports. So there's a footnote, and
8 Melanie will look it up for you.

9 But the -- anyway, the upshot of this is that we
10 think probably that we should be using an uncertainty
11 factor for the kinetic intraspecies components of 10
12 rather than 3.16. And this covers most, although not all,
13 of the examples we looked at. And we just see those ones
14 where it's greater than 10 as not unusual but at least the
15 more severe cases of the situation, and that we would hope
16 to identify those by specific analysis when we --

17 PANEL MEMBER BLANC: And on a theoretical basis,
18 how are you handling fetal exposures in these
19 conceptually?

20 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

21 CHIEF SALMON: We don't have a good handle on fetal
22 exposures. And the kinetics -- there are some kinetics
23 looking at uptake of xenobiotics by the fetus. But the
24 data are pretty limited and they typically don't deal very
25 well with the sorts of questions that you'd be concerned

1 about with, you know, the site of toxicity. You know, for
2 instance, it's not just how much gets into the fetus as a
3 whole, but how much gets into a specific area of the fetus
4 and what metabolic capabilities in that area are. So the
5 short answer is we -- at this point we don't really have a
6 very good handle on that.

7 PANEL MEMBER BLANC: But for this kind of
8 exercise, wouldn't it have made sense to see if the
9 same -- whether the range is yet even greater?

10 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

11 CHIEF SALMON: If we had the means to do that, yes. But I
12 don't think at this point we have the means to do it.

13 PANEL MEMBER BLANC: Meaning there are no
14 examples of chemicals for which you have fetal data?

15 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

16 CHIEF SALMON: There are no good models that I'm aware of
17 where we could use that. But I don't know -- you know, I
18 mean -- you know, let's say that certainly if we came
19 across an example where we had such a model, obviously
20 that would be very interesting. But I'm not aware of a
21 case where we have one that we could use in this way.

22 The objective here was primarily to determine the
23 range of the uncertainty factor for the intraspecies
24 extrapolation. So for that uncertainty factor, we're
25 actually looking at, you know, how would we extrapolate

1 the concentration to exposure of that individual? The
2 question of, you know, what's the exposure to the fetus
3 via the mother is a much -- certainly a much more
4 complicated issue. And I think the only good answer that
5 we have at this point that is to say that we would hope to
6 look at developmental studies.

7 PANEL MEMBER BLANC: No, but maybe I didn't
8 understand what you did. I thought for this table you
9 took examples of chemicals for which you had a series of
10 data on the effects -- or the pharmacodynamics --

11 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
12 CHIEF SALMON: On the kinetics, yes.

13 PANEL MEMBER BLANC: On the kinetics on these
14 various age ranges.

15 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
16 CHIEF SALMON: Yes.

17 PANEL MEMBER BLANC: And you showed what the
18 difference in the area under the curve was or some
19 integrated measure and then saw how different it was and
20 you divided the range -- and you present the range here,
21 isn't that right, by category?

22 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
23 CHIEF SALMON: Yes, that is correct. But we don't at this
24 point have the technical means to produce a very
25 satisfactory answer for the fetus.

1 CHAIRPERSON FROINES: Well, how did you come up
2 with the ultra factor -- the UF factor being greater than
3 10 for methylene chloride?

4 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

5 CHIEF SALMON: By fitting a combination of measures and
6 extrapolated infant-specific parameters into the PBPK
7 model.

8 PANEL MEMBER BLANC: Well, I should think that
9 something that would be of use in this would be looking
10 and seeing what happens with carbon monoxide, since you do
11 have fetal data on that.

12 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

13 CHIEF SALMON: Yes. Although I think there are --

14 PANEL MEMBER BLANC: I mean there must be some
15 other examples then.

16 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

17 CHIEF SALMON: There's not very much that we could use in
18 the sense of having enough coverage to be able to produce
19 a prediction of a usable default at this point. I think
20 that's the object -- that was the overall objective of
21 this exercise.

22 PANEL MEMBER BLANC: Well, wasn't the -- I
23 thought the object was to show that there's enough things
24 that fall beyond a default of 3 that that wouldn't be
25 public health protective on an automatic basis.

1 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
2 CHIEF SALMON: Yes. And I think we have covered
3 sufficient number of examples to demonstrate that. But
4 there are clearly going to be many other specific cases of
5 interest. But, as I say, as a general rule, I think it's
6 fair to say we don't have as satisfactory and complete a
7 kinetic model available of fetal exposures to be able to
8 include consideration of that for this purpose.

9 --o0o--

10 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
11 CHIEF SALMON: Now, one of the key things that we were
12 concerned about was this question of target organ
13 sensitivity and the fact that the dividing and
14 differentiating cells in children may be more sensitive to
15 damage. So I think this is another -- I mean we've been
16 talking about the kinetics. But now we're talking about
17 things that might affect the toxicodynamics.

18 --o0o--

19 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
20 CHIEF SALMON: So going on to consideration of
21 toxicodynamics, there are certainly reasons for thinking
22 that children may be more -- actually more sensitive at
23 the tissue level target organ sensitivity. And this
24 should -- by the way, I'm sorry, there's a typo in the
25 title. That should read "toxicodynamic variability."

1 That's what I'm talking about here.

2 PANEL MEMBER HAMMOND: Shouldn't that be UFH-d?

3 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

4 CHIEF SALMON: That should be UFH-d, yes. I'm sorry, the
5 title got copied across and then it didn't get edited. It
6 should have been.

7 So we have a position that children may be more
8 sensitive to toxicity than adults. But in general -- I
9 mean and certainly there are specific cases where we know
10 about this. But in general we lack quantitative
11 information on how large that difference would be. And we
12 have in the past assumed that the existing defaults is
13 adequate. And in this particular context we are going
14 to -- we're proposing to assume that the existing default
15 is adequate, because we don't have evidence in general
16 that it's insufficient. But we do recognize that there
17 are some specific organ systems and toxic endpoints which
18 have been identified as being of particular concern. And
19 these -- this is a list of some of the, so to speak, red
20 flag effects, which we particularly identified these in
21 our SB 25 prioritization, for instance.

22 So these are things that we would tend to look at
23 and say we think there's a potential for infants to be
24 more sensitive -- quite apart from any kinetic
25 differences, they would be more sensitive at the tissue

1 levels of these kinds of effects.

2 --o0o--

3 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

4 CHIEF SALMON: And what we hope of course is --

5 CHAIRPERSON FROINES: Andy, go back a second.

6 You don't think that respiratory disorders

7 shouldn't be in there?

8 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

9 MARTY: They are. We put those in there in our
10 prioritization document. I mean we -- this is not a
11 complete list, for sure. The one example that we gave
12 during the prioritization process was asthma as
13 differentially impacting young children.

14 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

15 CHIEF SALMON: I think that one got kind -- because this
16 slide has only so much space, that probably got subsumed
17 under the immunotoxicity heading. But it's certainly a
18 substantial consideration and one which we hope -- you
19 know, we intend to give full attention to.

20 So, anyway, what we're saying is, firstly,
21 therefore, what we propose is that we would use a
22 toxicokinetic component uncertainty factor for
23 intraspecies extrapolation of 10 as a default, and that we
24 would use -- the uncertainty factor for extrapolation of
25 toxicodynamics, the default we would use is 3 or 3.16.

1 This would in fact increase the overall intraspecies
2 uncertainty factor to a total of 30 by default.

3 PANEL MEMBER BLANC: Thirty-one actually.

4 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
5 CHIEF SALMON: Well, no -- oh, yes, 31.6 if you -- but the
6 trouble is, yeah, we keep getting beaten up if we quote
7 more than one significant figure. So this is why there's
8 this constant flip-flop between is it 3 or is it 3.16 and
9 powers of 10 beyond that.

10 PANEL MEMBER BLANC: Well, except here you're
11 multiplying it then again by 10. So it's not so trivial a
12 question.

13 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
14 CHIEF SALMON: Yes. The answer is in every case when we
15 do the multiplication, we will use the true value of the
16 square root of 10 and we'll then round to one significant
17 figure.

18 PANEL MEMBER BLANC: Okay.

19 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
20 CHIEF SALMON: That's the procedure as defined.

21 PANEL MEMBER BLANC: Okay.

22 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
23 CHIEF SALMON: And so what we're saying, these would be
24 the defaults, which we would use unless we have evidence
25 to show otherwise or the ability to conduct an actual

1 model that would include appropriate infants and
2 children's parameters.

3 PANEL MEMBER BLANC: So if I understand you
4 correctly, this is actually a major policy change.

5 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

6 CHIEF SALMON: Yes. This is the bigger -- one of the
7 bigger changes that we're proposing, definitely.

8 PANEL MEMBER BLANC: And this will put you quite
9 a bit at a divergence from current EPA policy.

10 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

11 CHIEF SALMON: Well, of course it depends which piece of
12 EPA you're talking about, in that by doing this we're
13 actually halfway between what the air program is doing,
14 which I think is essentially not much at this point, and
15 what they're doing under the FQPA factor, which is putting
16 in a whole factor of 10 in addition, which I'm not saying
17 covers only this or with this sort of compound. But, you
18 know, for the pesticide area they're potentially talking
19 about needing an additional factor of 10 rather than 3.
20 But that --

21 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

22 MARTY: Also, I think it's fair to say that EPA has added
23 additional uncertainty factors where they felt there was a
24 need -- there was a data deficiency, and primarily where
25 there was a data deficiency in developmental toxicity. So

1 they have done that on many occasions.

2 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

3 CHIEF SALMON: Yeah, that's -- well, I'm going to say a
4 little bit more about that in a moment.

5 But it certainly -- it's not the case that EPA
6 has ignored this problem. But they have in fact -- you
7 know, they've taken assessment-specific choices to address
8 it rather than at this point having a policy default.

9 But you're right. This is the -- probably the
10 largest single change we're proposing and also the one
11 which has attracted a lot of comment.

12 --o0o--

13 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

14 CHIEF SALMON: Melanie mentioned the data deficiency
15 uncertainty factor. This is something which --

16 CHAIRPERSON FROINES: You say it's generating a
17 lot of comment. Are we seeing those comments coming in,
18 or what's the situation?

19 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

20 MARTY: We're in the process of responding to those
21 comments and, if appropriate, revising the document. So
22 the next thing the Panel will see is a revised document
23 plus the comments and our responses to those comments.

24 CHAIRPERSON FROINES: And that you think is?

25 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

1 MARTY: It would be certainly before the next meeting,
2 which we're hoping is two months.

3 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

4 CHIEF SALMON: So U.S. EPA has used this concept of the
5 data deficiency uncertainty factor in a variety of cases.
6 And they've certainly used it in cases where they were
7 concerned about impacts on infants and children. But one
8 of the most important areas is not only postnatal but
9 prenatal developmental toxicity.

10 We have not used this factor in previous OEHHA
11 guidelines. But we now see it as a useful addition,
12 especially to address concerns for children's health. And
13 we feel that it would be useful to include this as a
14 policy option where we have concerns about developmental
15 impacts, including the kind of concerns about prenatal
16 exposures and the difficulties that we have in dealing
17 with, for instance, the kinetic uncertainties of fetal
18 exposure, which Dr. Blanc pointed out to us just now.

19 So this is one way that we would perhaps want to
20 build in additional uncertainty to address things that we
21 can't necessarily model well.

22 And of course what we hope is that we would have
23 actual toxicological data which would address this
24 concern. But where we lack that data, we propose to use
25 this data deficiency uncertainty factor similarly to the

1 way it's been used recently by U.S. EPA.

2 PANEL MEMBER BLANC: But I think what's getting
3 confusing here is what you're -- what you've said
4 previously is that the intraspecies factor could be as
5 large as 30 if you have no data at all upon which to make
6 any estimate of the toxicokinetic or toxicodynamic --

7 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

8 CHIEF SALMON: Yes.

9 PANEL MEMBER BLANC: And now you're saying that
10 in addition it might be three times greater, it might be
11 90 in the case in which you don't have data, but you've
12 already said that the reason you'd have the value of 30 is
13 because you don't have any data. So how much more data
14 can't you have?

15 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

16 CHIEF SALMON: Well, the 30 reflects the situation where
17 we're using 10 to address the uncertainty in kinetics.
18 But we're still only using 3.16 to address the uncertainty
19 in toxicodynamics. So this would come in, for instance,
20 in a case where we've got toxicity studies in adult rats
21 which identify a particular kind of endpoint, you know,
22 say, respiratory irritation or something like that, but we
23 don't have studies either in young humans or young
24 animals, and we're concerned that there's a possibility of
25 a different toxicodynamic result. You know, that would be

1 one case where --

2 PANEL MEMBER BLANC: But isn't that where the 3.1
3 comes from?

4 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF
5 MARTY: Yeah, I think what this is trying to do to have a
6 data deficiency uncertainty factor is make it for the fact
7 where you really have huge data gaps and that you have a
8 suspicion that this thing might be worse from a dynamic
9 aspect in early life stages. Then you can have a higher
10 uncertainty factor than just the -- higher cumulative
11 uncertainty factor than just the 30X for intraspecies.
12 You could add an additional database deficiency.

13 PANEL MEMBER BLANC: I understand what you're
14 saying. I think I'm having difficulty understanding some
15 examples that would help me pinpoint a scenario in
16 which -- because you're basically having two classes of
17 uncertainty. There's an uncertainty that I don't really
18 care about and then there's an uncertainty that I'm
19 really -- you know, I'm sort of uncertain and now I'm
20 really, really, really uncertain or something like that.
21 Because in the EPA versions since they don't have the
22 tenfold, basically they could get up to 30, which is where
23 you are as a sort of baseline, right? They could get up
24 to the same value as you if they put in the threefold
25 uncertainty factor.

1 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

2 CHIEF SALMON: They could put in -- and actually they
3 could if they chose to, put in an uncertainty factor of 10
4 as well, you know. These are all default values depending
5 on the case. But, yes --

6 PANEL MEMBER BLANC: Well, I understand that.

7 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

8 CHIEF SALMON: If I -- can I --

9 CHAIRPERSON FROINES: What we don't understand is
10 this factor of 3 -- UFD 3.

11 PANEL MEMBER HAMMOND: Is that for developmental
12 specifically or is it for --

13 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

14 CHIEF SALMON: No, it's not exclusively for developmental.
15 But we -- what we're saying here is that that is probably
16 the most likely -- what we're saying is in general we
17 would want the ability to apply an uncertainty factor to
18 reflect concerns where we feel that there's something
19 which is not covered by the available data. And if I can
20 give you just an example of how this might play out.

21 Supposing for the sake of argument we have a
22 solvent which causes respiratory irritation. We're trying
23 to set a REL which is going to be applicable to not only
24 adults but infants and children. We only have a study in
25 animals, say, or in humans, for that matter, if -- say

1 it's a worker study, we have a study which tells us what
2 is the critical exposure in an adult mortal exposure.

3 So we look at that. We apply a tenfold UFH-k
4 because our study is in healthy adults. And we feel that
5 we need that thirtyfold uncertainty to extrapolate the
6 kinetic uncertainty to infants and children.

7 But then we also realize that this particular
8 solvent has some central nervous system effects. Perhaps,
9 you know, in adults those are happening at about the same
10 level as all the other things we're looking at. So they
11 won't necessarily, the critical effect even in the adult.
12 But in any case, if we're looking at this neurotoxicity in
13 the adult, it's going to be expressed by, you know,
14 anesthesia, possibly nausea, and effects on color vision
15 or something. But, anyway, some temporary reversible
16 neurotoxicity, which we certainly wouldn't ignore.

17 But if we look at the neurotoxicity of quite a
18 number of these things in infants and children, or at
19 least in infant rats, and if we look at what happens in in
20 utero exposure, we see that -- we're seeing things like
21 irreversible changes in neurotransmitters, we're seeing
22 persistent behavioral alterations in the exposed offspring
23 and things like that. So that's actually a different and
24 significantly more sensitive endpoint than the things that
25 we're seeing in the adults.

1 So then what we're saying is in this particular
2 compound, we've got the adult numbers, we've done all the
3 usual things and we've got what we think is going to be a
4 reasonable protective level based on those adult effects,
5 but we suspect based on the nature of the toxicity and so
6 on that there may be in this case, say, a
7 neurodevelopmental effect to which the fetus or the infant
8 in particular is going to be much more sensitive. And
9 because we don't have any data about that at all, we're
10 concerned about it.

11 And so we're proposing to use this UFD to add in
12 an extra safety factor to provide an extra degree of
13 protection against that possibility. That would be the
14 kind of example that we'd be thinking of.

15 Does that make sense?

16 CHAIRPERSON FROINES: No.

17 PANEL MEMBER BLANC: Well, what I have to say is
18 that I think it's -- in principle I think you should have
19 a safety valve that would allow you to be more
20 conservative in situations where you think the stakes are
21 higher and by --

22 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

23 MARTY: That's really what this is.

24 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

25 CHIEF SALMON: That's what it is.

1 PANEL MEMBER BLANC: -- and by analogy. But I
2 think that for the sake of consistency and transparency
3 and understandability down the road, so that when it comes
4 to the point where there's a critical toxicant for which
5 in fact it's because you chose a ninetyfold safety factor
6 that it has sort of public policy -- potential public
7 policy implication in terms of how many hot spots are
8 exceeding -- likely to exceed your REL, you are going to
9 have to have a better explication of your rationale.

10 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

11 MARTY: Well, we would on -- yeah, in any specific
12 chemical toxicity summary we go through why we've applied
13 that.

14 PANEL MEMBER BLANC: I understand that. But I
15 think in your master document you perhaps should think
16 through how to tighten your description of the safety
17 valve. And I do think that you're on firmer ground when
18 you're talking about, you know, developmental issues. And
19 I think that -- you know, Kathy mentioned earlier the sort
20 of generic issue of CNS toxins and the presumed risk that
21 develop in nervous system in that situation. And there
22 could be some other examples. But I think I would go
23 back, look at it carefully, and make sure that your
24 generic argument is as clear-cut as it can be.

25 You know, in a way what you're actually saying is

1 that, not that it's a threefold uncertainty factor, but in
2 fact you're substituting a factor of 10 for the
3 toxicodynamics with a factor of 30.

4 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF
5 MARTY: Yes.

6 PANEL MEMBER BLANC: That's really what you're
7 saying. And that to me would make more sense as the
8 argument.

9 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF
10 MARTY: And, in fact, that's what we explain in a few of
11 the sample RELs. There are a few where asthma was a
12 concern. They're respiratory irritants. They're known to
13 trigger asthma. Asthma's the worst disease in kids. So
14 we added an additional uncertainty factor for that.

15 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
16 CHIEF SALMON: But I think the difference between
17 increasing the value of the UFH-d as opposed to putting in
18 this data deficiency factor -- no, the distinction as I
19 see it is on the one case we're looking at a measured
20 endpoint which is -- you know, for which we have some
21 data, say, in adults but we suspect that the children will
22 be more sensitive to that endpoint. Whereas, the purpose
23 of the data deficiency uncertainty factor is to also
24 address a consideration where we think we know something
25 about the endpoint we see in adults. And we don't

1 necessarily have to be able to say that the children are
2 going to be dramatically more sensitive to that endpoint.
3 What the UFD here is addressing is the case where we
4 suspect there may be another and different endpoint.
5 That's the difference between increasing UFH-d and
6 then the case where we would optionally where we had that
7 concern.

8 PANEL MEMBER BLANC: Well, is that true for the
9 four chemicals which in your previous table had the
10 uncertainty factors greater than 10. Were those in fact
11 uncertainty factors that came out to be greater than 10
12 because there was a different end organ?

13 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
14 CHIEF SALMON: No.

15 PANEL MEMBER BLANC: Or was the very same --

16 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
17 CHIEF SALMON: Those greater than 10 are purely the
18 kinetic component. They're not about what we're
19 discussing here at all.

20 CHAIRPERSON FROINES: Yeah, they would have to be
21 greater than 30.

22 PANEL MEMBER BLANC: Oh, I'm sorry. You're
23 right, greater than 3 to --

24 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
25 CHIEF SALMON: Yeah, but that table is about kinetics

1 only.

2 PANEL MEMBER BLANC: Right, right. I'm sorry.

3 I see. So --

4 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

5 CHIEF SALMON: It's conceivable that we would have, you

6 know, a value of -- an overall value of UFH. The

7 intraspecies factor could go as high as a hundred due to

8 selection of larger factors than default or based on

9 evidence or concerns.

10 CHAIRPERSON FROINES: I understand. But I'm very

11 curious to see an example at some point, because I think

12 that it's very vague at some level. But it's sort of

13 rhetorical --

14 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

15 CHIEF SALMON: Yes, I think the problem with this is this

16 is not something that we're doing all the time. It's

17 something which we are proposing as an option to be

18 available in specific cases. And the specific -- you

19 know, the justification for using it would necessarily

20 have to be presented in the specific case where it would

21 be applied.

22 PANEL MEMBER HAMMOND: But, you know, I think many of us

23 understand what you're struggling -- you're struggling

24 with something that we're also struggling with. But there

25 is that sense of, first, the term "data deficiency," you

1 know, when Paul started out talking about, "Well, isn't
2 that data deficiency you're talking about in the other
3 factors?" And they are data deficiencies, right? I mean
4 that's why you have the uncertainty factors for the K and
5 the D.

6 And then it turns out sometimes it's the
7 endpoint, we're looking at a particular endpoint where we
8 know that the child is more sensitive. So that's a
9 different kind of reasoning. And at some level you're
10 saying there are many reasons that we might need to do
11 that. And I think we agree, but I think that that
12 probably needs be more carefully articulated.

13 CHAIRPERSON FROINES: Well, I think it needs to
14 be carefully articulated because somebody who is in your
15 opposition is going to focus on it. And it's going to
16 have a -- it's going to have a potentially negative impact
17 in terms of how OEHHA is seen in terms of uncertainty
18 factors.

19 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
20 CHIEF SALMON: Well, I think there's a clear intention to
21 only use this additional factor, you know, when we can
22 provide a rational case-specific narrative to defend it,
23 which would go some way to -- you know, to address --

24 PANEL MEMBER HAMMOND: You know, maybe -- in that
25 case I would suggest maybe you in fact say that

1 explicitly, that there could be uncertainty factors for
2 other cases that are carefully explicitly laid out. In
3 which case you may not want to say that the default value
4 is 3. You may actually want to pick up of the value that
5 seems appropriate for the type of outcome you're talking
6 about or whatever the reason is for that uncertainty
7 factor.

8 So you might want to rather say there are many
9 reasons -- there are other uncertainties that enter. Talk
10 about some of those, talk about what you know about those,
11 and say that if one were to introduce another uncertainty
12 factor, you would have to have a strong case made in any
13 particular case. So you might leave the door open that
14 way. But I think leaving it open in this kind of there's
15 going to be a defined default of 3 for multiple reasons
16 that could be there, and it begins to seem like, "well, I
17 just want to have this extra thing in my back pocket."

18 CHAIRPERSON FROINES: Andy, you know what I think
19 would be useful -- and I'll take you at your word here.
20 You say on the slide used by U.S. EPA for some time, more
21 recently with clearer criteria. So that means to me that
22 there are some examples.

23 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
24 CHIEF SALMON: Yes, there are.

25 CHAIRPERSON FROINES: And it would be useful if

1 we saw one or two of those examples, because that gives
2 the impression that it's not yet to come.

3 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

4 CHIEF SALMON: Yeah.

5 PANEL MEMBER BYUS: And I do think in the written
6 document, which is clear, you can sense this, your
7 language has to be a lot more precise than you're saying
8 right now. I mean incredibly more precise. And I mean if
9 you want feedback, that's the feedback I'm going to give
10 you.

11 So I mean I think all of this is well and good.
12 I mean I think it's well intentioned. I agree with all
13 the premises that you've laid out. I just think the
14 language that you've presented today is soft. And if you
15 write it that way, it's not going to carry water. So
16 let's hope that the written document is much more
17 carefully constructed and the language is very precise.
18 And I agree with John, some examples -- and you tried to
19 give us one off the top of your head, and I don't think
20 that maybe you -- but an example or two or three as you're
21 going along is also a good way to clarify the precision of
22 what you're saying.

23 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

24 MARTY: Yeah. The only thing I would say to that is, you
25 know, we have to -- if you get overly precise, you paint

1 yourself in a corner. And it really --

2 PANEL MEMBER BYUS: But the language has to be
3 clearer than what you're saying. Much clearer. You know,
4 we're all university faculty. We live by these words,
5 papers, manuscripts, whatever, teaching, lectures. Words
6 are very, very precise. And I think -- as I said, I
7 understand the premises here. I think they're all well
8 and good. I think you're really -- this should definitely
9 be done. And I tend to agree with you. But the language
10 is what's bothering me.

11 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF
12 MARTY: Okay.

13 CHAIRPERSON FROINES: Well, in the long run
14 it's going -- it seems to me to have -- you know, we're
15 supposed to separate risk assessment from risk management.
16 But if I had something -- if you came in to something and
17 you said to me, "This chemical X has to have an
18 uncertainty factor of 100," I would say maybe we should
19 consider not using that chemical in California, because
20 it's probably very, very toxic. And so it's -- the risk
21 management issue is not trivial when you've got something
22 that obviously has -- you felt compelled to come up with
23 numbers like you're talking about.

24 Although we're talking about data deficiency, so
25 it's not necessarily -- that's the contradiction, isn't

1 it.

2 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

3 CHIEF SALMON: Well, maybe one of the things we can do is
4 actually dig out what U.S. EPA currently says about this
5 one, because they -- I say they have in fact been doing
6 this for some time. And some of the things which I've
7 attempted to lay out, obviously unsuccessfully here, are
8 based on what they've actually been doing. So --

9 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

10 MARTY: Well, we'll go back and look at the language.

11 PANEL MEMBER BLANC: But again if I understand
12 the context of the EPA doing it, EPA is doing it in a
13 situation where otherwise their default value would be 10.

14 CHAIRPERSON FROINES: Right.

15 PANEL MEMBER BLANC: And this uncertainty factor
16 brings them only up to where you are at your default
17 level. And this is part of what triggered my line of
18 questioning. So when you do this new uncertainty factor
19 of 3, it's going to take you from a default level, which
20 is actually the maximum except in some extraordinary
21 circumstance for the EPA, and you're going to be then
22 three times higher than that. Right?

23 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

24 MARTY: Possibly. It really -- it very much depends on
25 how they've interpreted the data.

1 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
2 CHIEF SALMON: The other thing we're proposing as a change
3 is that the Haber's Law adjustment -- this is again
4 something which we have been doing in the past. It's a
5 way -- essentially when considering acute exposures, the
6 general finding is that in fact concentration is more
7 important than duration as a factor in determining the
8 extent of result.

9 The concern is how do you extrapolate from the
10 duration of an experimental acute tox study to the
11 one-hour period of interest for an acute reference
12 exposure level.

13 We've done this before. This so-called modified
14 Haber's Law uses an exponent of N, which is a weighting of
15 the concentration term. The default we used previously
16 was 2. But we're now proposing to change this default to
17 3, which increases the weight of the concentration term
18 relative to the time term. This is consistent with what
19 U.S. EPA now does and also consistent with the more
20 extensive data which are now available.

21 The value of N has in fact been determined for
22 quite a number of these chemicals. So there's a known
23 range of values of various specific chemicals. And where
24 we had a measured value, obviously we'd use it. But we're
25 talking about what's a good default here.

1 from the previous document.

2 The timetable for what's been going on and what's
3 proposed here: This draft has been reviewed by the Air
4 Resources Board and CAPCOA. The public comment period, as
5 you've heard earlier, has taken place and has been
6 extended until quite recently.

7 We're starting your review with this meeting.
8 And we are obviously looking at a subsequent meeting when
9 you will see not only responses to the public comments but
10 also, as far as we can, initial responses to your comments
11 today. And with a view to potentially winding this up
12 some time in the middle of this year.

13 And we've also developed some new RELs which
14 we're not going to be able to deal with today. But you'll
15 hear about those in due course as examples of this
16 process.

17 CHAIRPERSON FROINES: Is this list those new RELs
18 that we're not hearing about today and that you want lead
19 Panel members on?

20 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

21 MARTY: Yes.

22 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

23 CHIEF SALMON: That is right, yes.

24 CHAIRPERSON FROINES: And so that's -- would
25 those RELs come up in mid-2008?

1 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

2 MARTY: Yeah, they're -- you should have copies of them
3 already in the materials that you received. So hopefully
4 then at the next meeting we'll be able to get more into
5 the meat of what we just presented as well as the actual
6 chemicals.

7 CHAIRPERSON FROINES: So, Melanie, when do you
8 intend to bring the cancer methodology to us?

9 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

10 MARTY: It's about to undergo internal ARB review. Then
11 next month in April we'll start a public comment period.
12 We'll have to do at least 60 days. Then we respond to
13 comments and then we send it to the Panel. So it sounds
14 like to me fall for you guys to be looking at that

15 CHAIRPERSON FROINES: So when we talk about lead
16 persons, we don't need to actually -- do we need to assign
17 somebody, person or persons, for that now or should we
18 just deal with this?

19 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

20 MARTY: That would be great if you can assign people for
21 the cancer document now.

22 CHAIRPERSON FROINES: Now.

23 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

24 MARTY: Yeah, that would be good.

25 PANEL MEMBER BYUS: The non-cancer document? Or

1 is it cancer --

2 CHAIRPERSON FROINES: No, the cancer document.

3 PANEL MEMBER BYUS: I'm confused.

4 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

5 MARTY: John's talking about the next document.

6 PANEL MEMBER BYUS: Oh, I'm sorry.

7 CHAIRPERSON FROINES: The next document that's

8 coming down the road.

9 PANEL MEMBER HAMMOND: But we haven't assigned

10 these -- for these yet.

11 CHAIRPERSON FROINES: I know.

12 PANEL MEMBER HAMMOND: But the non-cancer

13 document.

14 CHAIRPERSON FROINES: I'm trying to look at the

15 whole panoply of work.

16 PANEL MEMBER BYUS: John's way ahead of us, as

17 usual.

18 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

19 MARTY: So I should say, because the other Panel members

20 may not know, but Stan Glantz was the lead on this current

21 non-cancer REL document.

22 PANEL MEMBER HAMMOND: Oh, we did have a lead.

23 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

24 MARTY: Yes. And so we worked a little bit with him

25 already. But he -- typically for the individual chemicals

1 we've had additional leads.

2 CHAIRPERSON FROINES: Well, doesn't it make sense
3 to assign Stan, since he's not here --

4 (Laughter.)

5 PANEL MEMBER BYUS: Yeah, I like that.

6 CHAIRPERSON FROINES: -- for the cancer document
7 and assign Joe, since he's theoretically an oncologist,
8 for the cancer document? And then 1, 2, 3, 4, 5, 6 --
9 there are six here, so everybody should take one.

10 PANEL MEMBER BLANC: Which one -- I would like to
11 do manganese myself.

12 PANEL MEMBER HAMMOND: I'd like to do manganese.

13 CHAIRPERSON FROINES: I knew you'd like -- wait.

14 PANEL MEMBER PLOPPER: You know, and I'll take
15 the formaldehyde.

16 CHAIRPERSON FROINES: Charles is formaldehyde.
17 Paul is manganese.

18 PANEL MEMBER FRIEDMAN: Which one has the most
19 epidemiologic data? That's the one I would like to take.

20 CHAIRPERSON FROINES: Well, certainly arsenic.

21 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF
22 MARTY: Arsenic.

23 PANEL MEMBER FRIEDMAN: How about if I take that
24 then?

25 CHAIRPERSON FROINES: Arsenic is more -- has

1 enormous amount of -- and so that leaves acetaldehyde,
2 acrolein, and mercury. And we're missing --

3 PANEL MEMBER FRIEDMAN: I'll do one, whichever
4 one you want.

5 CHAIRPERSON FROINES: Pick one.

6 PANEL MEMBER BYUS: And I'll do acrolein, unless
7 you want it.

8 CHAIRPERSON FROINES: I'd rather do acrolein than
9 mercury. How about taking mercury?

10 PANEL MEMBER BYUS: You want me to take mercury?

11 CHAIRPERSON FROINES: Uh-huh.

12 PANEL MEMBER BYUS: All right. I'll take
13 mercury.

14 CHAIRPERSON FROINES: And I'll take acetaldehyde
15 since I'm the air pollution guy here.

16 PANEL MEMBER BLANC: You're taking two.

17 CHAIRPERSON FROINES: Oh, wait. Kathy. What did
18 I almost do?

19 So you're acrolein or acetaldehyde.

20 PANEL MEMBER HAMMOND: You take which one you
21 want. I'll take the other one.

22 CHAIRPERSON FROINES: No, no. You take what you
23 want.

24 (Laughter.)

25 PANEL MEMBER HAMMOND: I said manganese.

1 CHAIRPERSON FROINES: Yeah, but he's got a thing
2 about manganese.

3 PANEL MEMBER HAMMOND: I do -- research on that.

4 CHAIRPERSON FROINES: Oh. Well, what do you want
5 to do? Do you want --

6 PANEL MEMBER HAMMOND: I'll do -- which one did
7 you want to take?

8 CHAIRPERSON FROINES: Well, I don't care what I
9 do.

10 PANEL MEMBER BLANC: Who's doing formaldehyde?
11 Did I miss that?

12 CHAIRPERSON FROINES: Charles.

13 PANEL MEMBER BYUS: Which ones have the biggest
14 changes in the RELs?

15 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
16 CHIEF SALMON: Acrolein is one of the bigger ones
17 actually.

18 PANEL MEMBER FRIEDMAN: Are the documents the
19 ones that are in this book that you'd like us to review?

20 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
21 CHIEF SALMON: Yes, they are.

22 CHAIRPERSON FROINES: And I'm acetaldehyde.

23 So you realize that the acrolein one you have to
24 do EGFR activation, you know, for the endpoint. You don't
25 get to use these old fashioned endpoints. You have to do

1 PTP1B inactivation.

2 PANEL MEMBER HAMMOND: Maybe you should pick the
3 lead on that.

4 PANEL MEMBER BLANC: Let me just -- coming back
5 to the topic that we beat to death about uncertainty.
6 Let's just take for a moment arsine, which is a subset of
7 arsenic, which causes hemolysis. And neonates deal very
8 poorly with hyperbilirubinemia. So that's something you
9 took into account in some kind of uncertainty factor?

10 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
11 CHIEF SALMON: Actually the way the arsine data worked, we
12 looked at the hemolysis data and we also looked at a
13 number of endpoints including data from the epidemiology.
14 And that covered -- the other endpoints were all very
15 considerably more sensitive than the hemolysis data that
16 we had. So hemolysis -- so what we basically said was
17 that we needed to use the all-arsenic endpoints for arsine
18 rather than looking at hemolysis as the critical endpoint
19 for arsine.

20 PANEL MEMBER BLANC: For acute effects?

21 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION
22 CHIEF SALMON: Yeah.

23 PANEL MEMBER BLANC: That seems biologically
24 implausible to --

25 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

1 CHIEF SALMON: Well, that was -- I'll have a look and
2 see -- you know, I don't think we --

3 PANEL MEMBER BLANC: I don't want to dwell on it
4 now. I just pick as --

5 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

6 CHIEF SALMON: Yeah. But the answer is we considered a
7 range of endpoints definitely.

8 PANEL MEMBER HAMMOND: May I ask, are you
9 expecting the REL documents to change as you do the
10 changes for the overall approach document?

11 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

12 CHIEF SALMON: We have not got -- well, we've not got
13 anything in line at this point. There might be some
14 corrections or -- the other thing is we might, I suppose,
15 need to consult with the leads if we identify a problem
16 through the public comments.

17 PANEL MEMBER HAMMOND: So you've received -- and
18 that's what this is. You've received public comments on
19 all of these?

20 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

21 CHIEF SALMON: Yes.

22 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

23 MARTY: Yes.

24 PANEL MEMBER HAMMOND: So there may be changes in
25 these documents?

1 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

2 CHIEF SALMON: It' conceivable, yes.

3 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

4 MARTY: Yes.

5 CHAIRPERSON FROINES: Well, these are interesting
6 compounds.

7 PANEL MEMBER BLANC: These are the ones that made
8 it on to that top list, right? Isn't that where we're
9 going back to?

10 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

11 CHIEF SALMON: Well, all except acetaldehyde are somewhere
12 in the first or second tier of the SB 25 prioritization.
13 So that's certainly, you know, one key reason why these
14 were selected. The other was -- there was a degree of, we
15 selected ones which we felt exemplified principles or
16 problems that we wanted to exercise the new guidelines
17 with.

18 PANEL MEMBER BLANC: Okay.

19 PANEL MEMBER HAMMOND: Are the guidelines likely
20 to change in any way that would lead to changes in the
21 RELs?

22 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

23 CHIEF SALMON: Well, that may be up to you.

24 (Laughter.)

25 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

1 MARTY: Yeah, that -- yeah, we would have to be iterative,
2 because if the -- if you guys want changes to the
3 guidelines or somebody brings up some important points in
4 the public comment period that result in a change, then we
5 would have to see how that reflects on the individual
6 reference exposure levels. It may or may not, depending
7 on what the change is.

8 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

9 CHIEF SALMON: Yeah, but clearly --

10 PANEL MEMBER HAMMOND: Now, the public comment
11 period closed four weeks ago though?

12 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

13 MARTY: Yes.

14 PANEL MEMBER HAMMOND: So you had a chance to at
15 least look at them?

16 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

17 MARTY: We've had a chance to look at them.

18 PANEL MEMBER HAMMOND: You don't have a sense yet
19 then how much they might change?

20 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

21 MARTY: I'd have to say, no, we don't have a sense.

22 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

23 CHIEF SALMON: No.

24 CHAIRPERSON FROINES: You don't have the what?

25 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

1 MARTY: We don't have a sense of how it's going to impact
2 the RELs at this point.

3 CHAIRPERSON FROINES: When would you like --
4 Peter just gave me a note essentially asking when the next
5 meeting should be. And it should be I think based on when
6 you're going to be comfortable having completed
7 everything.

8 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

9 MARTY: End of April would be great, or early May,
10 avoiding certain weeks that are bad.

11 CHAIRPERSON FROINES: And according to Peter, for
12 reasons I don't know, he said Bay Area.

13 PANEL MEMBER BLANC: Well, we were in Orange
14 County.

15 PANEL MEMBER HAMMOND: Southern California.

16 PANEL MEMBER BLANC: I guess it would be fair to
17 have it in the Bay Area.

18 CHAIRPERSON FROINES: And do we have a place in
19 San Francisco?

20 MR. MATHEWS: Not yet. I'm working on it.

21 CHAIRPERSON FROINES: So we'll plan the first two
22 weeks in May. And Peter can poll people. And we'll plan
23 to have it in San Francisco or Oakland.

24 You know, Stan's not here, so -- stan always
25 complains about Oakland meetings.

1 PANEL MEMBER BLANC: What about Stanford? Do you
2 have any facilities?

3 PANEL MEMBER FRIEDMAN: I'm, you know, a
4 consulting professor. I don't have a lot of clout there
5 in terms of --

6 PANEL MEMBER BLANC: But you have that nice
7 conference room.

8 MR. MATHEWS: I'll try it again.

9 PANEL MEMBER FRIEDMAN: Yeah. And you have to
10 deal with the administration, not with me.

11 MR. MATHEWS: Well, I've dealt with them on --

12 PANEL MEMBER BLANC: I mean it's just as close
13 for you from the airport.

14 CHAIRPERSON FROINES: Doesn't matter to me.

15 MR. MATHEWS: I'll give it a try.

16 CHAIRPERSON FROINES: So thank you, Andy. That
17 was -- this is going to be an interesting process.

18 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

19 CHIEF SALMON: A long, strange trip perhaps.

20 CHAIRPERSON FROINES: That's one of those
21 statements that says that everything's not quite perfect
22 but we're heading towards that.

23 PANEL MEMBER BLANC: Well, I'd like to make a
24 motion that we adjourn.

25 CHAIRPERSON FROINES: Yes.

1 PANEL MEMBER BYUS: Second.

2 PANEL MEMBER FRIEDMAN: May I ask a question?

3 Are we expected then to have reviewed and given
4 our feedback to the OEHHA with regard to these six
5 chemicals by then? Is that the plan or what?

6 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

7 MARTY: Yes.

8 CHAIRPERSON FROINES: Yes. But also the next
9 meeting we will be discussing the amongst the Panel are
10 our views of the document. So it's not one of those where
11 we walk in and vote, because we've had no -- we've had
12 limited discussion. And if there's no discussion, then
13 we'll just vote. But otherwise we'll have a --

14 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

15 CHIEF SALMON: We'll have to present public comments as
16 well.

17 PANEL MEMBER HAMMOND: My impression here though
18 is that these chemicals were chosen because they helped to
19 illustrate some of the issues and the challenges that lead
20 to the developing of the new document.

21 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

22 MARTY: Partially and --

23 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

24 CHIEF SALMON: That's one of the factors, yes.

25 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

1 MARTY: Partially because they were prioritized high when
2 we looked at children's health issues.

3 PANEL MEMBER HAMMOND: But they particularly
4 bring us -- we get to confront some of the children issues
5 by looking at these materials. So I do think this
6 question of its being an iterative process might -- that
7 sounds pretty likely. And I think that --

8 OEHHA AIR TOXICOLOGY AND RISK ASSESSMENT SECTION

9 CHIEF SALMON: Yes, absolutely.

10 PANEL MEMBER HAMMOND: -- how much we come to
11 conclusion by the next meeting with either the RELs or the
12 document is less clear to me, and that may take some time.

13 CHAIRPERSON FROINES: Melanie, I had a question
14 for you that is not meant as a criticism.

15 But when you talked about OEHHA's priorities for
16 chemicals that will come up in the future, maybe TACs or
17 whatever, you spent most of your time talking about what's
18 going on in Canada, if I remember correctly. But you
19 didn't -- you did not give very much in the way of
20 specific chemicals that you think would be appropriate.
21 When we have that meeting, can you give us some ideas of
22 where you are on that question?

23 Am I asking a difficult question?

24 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

25 MARTY: Yes, that's a difficult question. I mean I think,

1 you know, that we have our ideas of some chemicals that we
2 think are petty important and that should be looked at.
3 But, you know, it has to be integrated with ARB's process
4 of prioritization. So, you know, they have their
5 candidate list of TACs and the information that goes into
6 their prioritization process.

7 CHAIRPERSON FROINES: I don't know if I agree
8 with that. I would argue something different. I would
9 argue that you as scientists have views of what's
10 important. That has nothing to do with ARB's
11 prioritization process. If I talk about quinones, that's
12 because I'm a scientist who deals with quinones. And it
13 doesn't have anything to do with ARB. In fact, having
14 some fresh ideas outside their prioritization process may
15 be useful. They're not going to come up with ultrafines,
16 I guaranty it. I might.

17 And so the point is, why do we need to -- my
18 notion of putting this workshop together was to get
19 ideas -- to get scientific ideas, not necessarily
20 government. And then we have to figure out how the
21 science relates to the prioritization process. It seems
22 to me that that's a process that we have to talk about.

23 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF
24 MARTY: Well, you know, we have --

25 CHAIRPERSON FROINES: Tobi's going to have

1 compounds and so am I and so is Roger or Roger's
2 replacement.

3 OEHHA AIR TOXICOLOGY & EPIDEMIOLOGY BRANCH CHIEF

4 MARTY: We have a lot of ideas that we want to move
5 forward on. We don't have a lot of time or bodies. But,
6 you know, one is to look at what Canada did and how they
7 prioritized, and whether any of those chemicals would be
8 expected to be in the air. And the other is to look at
9 some of the work we've already done with atmospheric
10 transformation of emissions from tailpipes, run those
11 through SAR -- existing SAR models and see what little
12 flags pop up on some of those. We have not had the time
13 to do that yet.

14 So I don't know that we could do that between now
15 and May. But we can come up with additional ideas.

16 CHAIRPERSON FROINES: Well, we see you as, you
17 know, in general, as the lead agency on risk assessment.
18 And so getting some substantive ideas would be valuable.
19 And the timing doesn't have to be May, but it would be
20 useful. But also your thought process about approach.

21 PANEL MEMBER BLANC: Can we call the question?

22 There's a motion on the floor.

23 CHAIRPERSON FROINES: Well, are we
24 finished -- are there any other issues that we should
25 talk -- we should raise with OEHHA while we're here?

1 Anybody?

2 Okay. All in favor?

3 (Ayes.)

4 CHAIRPERSON FROINES: We're adjourned.

5 (Thereupon the California Air Resources Board,

6 Scientific Review Panel adjourned at 1:06 p.m.)

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